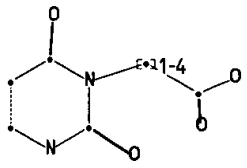
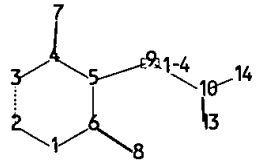
L Number	Hits	Search Text	DB	Time stamp
1	2240	((514/258.1) or (514/260.1) or (514/274) or (544/253) or (544/278) or (544/309) or (544/314)).CCLS.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/04/17 16:45

L Number	Hits	Search Text	DB	Time stamp
1	2240	((514/258.1) or (514/260.1) or (514/274) or (544/253) or (544/278) or (544/309) or (544/314)).CCLS.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/04/17 16:46
2	16277	convul$ or anticonvul$	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/04/17 16:46
3	11904	epilep$	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/04/17 16:46
4	2059	antiepilep$	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/04/17 16:46
5	24136	(convul$ or anticonvul$) or epilep$ or antiepilep$	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/04/17 16:46
6	88	(((514/258.1) or (514/260.1) or (514/274) or (544/253) or (544/278) or (544/309) or (544/314)).CCLS.) and ((convul$ or anticonvul$) or epilep$ or antiepilep$)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/04/17 16:46

C:\STNEXP4\QUERIES\09932676 (species).str

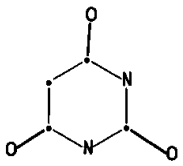


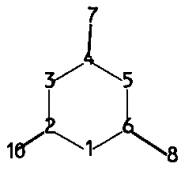


chain nodes :
7 8 9 10 13 14
ring nodes :
1 2 3 4 5 6
chain bonds :
4-7 5-9 6-8 9-10 10-13 10-14
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6
exact/norm bonds :
1-6 2-3 3-4 4-5 4-7 5-6 5-9 6-8 10-13 10-14
exact bonds :
1-2 9-10
isolated ring systems :
containing 1 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
13:CLASS 14:CLASS

C:\STNEXP4\QUERIES\09932676 (sub).str





chain nodes :
7 8 10
ring nodes :
1 2 3 4 5 6
chain bonds :
2-10 4-7 6-8
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6
exact/norm bonds :
1-2 1-6 2-3 2-10 3-4 4-5 4-7 5-6 6-8
isolated ring systems :
containing 1 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 10:CLASS

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=>
Uploading 09932676 (species).str

L1      STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1              STR
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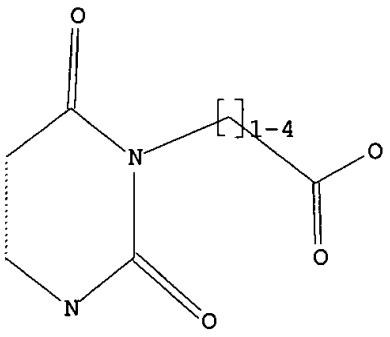


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Structure attributes must be viewed using STN Express query preparation.


=> s l1 sss sam
SAMPLE SEARCH INITIATED 14:29:06 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -   1120 TO ITERATE

 89.3% PROCESSED    1000 ITERATIONS                                 27 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:        20393 TO    24407
PROJECTED ANSWERS:             275 TO      933

L2           27 SEA SSS SAM L1

=> d his

     (FILE 'HOME' ENTERED AT 14:28:36 ON 17 APR 2003)

     FILE 'REGISTRY' ENTERED AT 14:28:42 ON 17 APR 2003
L1              STRUCTURE UPLOADED
L2           27 S L1 SSS SAM
L3          685 S L1 SSS FUL

=>
Uploading 09932676 (sub).str

L4      STRUCTURE UPLOADED

=> s l4 sub=l3 sss sam
SAMPLE SUBSET SEARCH INITIATED 14:31:17 FILE 'REGISTRY'
SAMPLE SUBSET SCREEN SEARCH COMPLETED -     15 TO ITERATE
```

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100.0% PROCESSED      15 ITERATIONS                              12 ANSWERS
SEARCH TIME: 00.00.01

PROJECTIONS (WITHIN SPECIFIED SUBSET):          ONLINE  **COMPLETE**
PROJECTED ITERATIONS (WITHIN SPECIFIED SUBSET):          68 TO      532
PROJECTED ANSWERS (WITHIN SPECIFIED SUBSET):             33 TO      447

L5           12 SEA SUB=L3 SSS SAM L4

=> s l4 sub=l3 sss ful
FULL SUBSET SEARCH INITIATED 14:31:25 FILE 'REGISTRY'
FULL SUBSET SCREEN SEARCH COMPLETED -    303 TO ITERATE

100.0% PROCESSED     303 ITERATIONS                             274 ANSWERS
SEARCH TIME: 00.00.01

L6          274 SEA SUB=L3 SSS FUL L4

=> s l3 not l6
L7          411 L3 NOT L6

=> s l7
L8          212 L7

=> s convul?
L9        21747 CONVUL?

=> s l8 and l9
L10           0 L8 AND L9

=> s epilep?
L11       15661 EPILEP?

=> s l8 and l11
L12           0 L8 AND L11

=> s seizur?
L13       18491 SEIZUR?

=> s l8 and l13
L14           0 L8 AND L13

=> s anticonv?
L15       20734 ANTICONV?

=> s l8 and l15
L16           0 L8 AND L15

=> s treat?
L17     2872160 TREAT?

=> s l8 and l17
L18          42 L8 AND L17

=> s weaver?
L19         872 WEAVER?
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=> s l8 and l19
L20             0 L8 AND L19

=> d l8 1-10 bib,ab,hitstr
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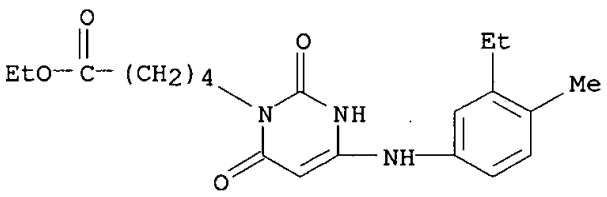
L8 ANSWER 1 OF 212 CAPLUS COPYRIGHT 2003 ACS
AN 2003:117630 CAPLUS
DN 138:170246
TI Preparation of N3-substituted 6-anilinopyrimidines to treat Gram-positive bacterial and mycoplasmal infections
IN Zhi, Chengxin; Long, Zheng-Yu; Wright, George E.; Brown, Neal C.
PA University of Massachusetts, USA; Shire Biochem Inc.
SO PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003011297	A1	20030213	WO 2002-US19398	20020617

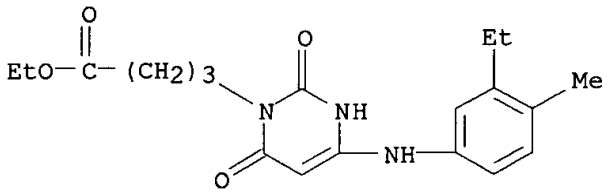
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-298357P P 20010615
US 2002-348420P P 20020114
OS MARPAT 138:170246
AB The title compds. [I; R1 = (CH2)m[An(CH2)p]qB (wherein A = CH2, CH:CH, CO, etc.; B = H, halo, alkyl, etc.; m = 1-4; n = 0-1; p = 0-4; q = 0-4); R2, R3 = alkyl, alkenyl, halo; or R2 and R3 together are alkylene; with the provisos], useful for treating Gram-pos. bacterial and mycoplasmal infections, were prepd. Thus, reacting 6-amino-2-methoxy-3-[2-(2-benzyloxyethoxy)ethyl]-4-pyrimidone with 3-ethyl-4-methylaniline.HCl afforded 72% I [R1 = (CH2)2O(CH2)2OCH2Ph; R2 = Et; R3 = Me] which showed MIC of 5 .mu.g/mL against S. aureus and E. fecalis.
IT **478921-24-3P**, 3-(4-(Ethoxycarbonyl)butyl)-6-(3-ethyl-4-methylanilino)uracil **480446-12-6P 496942-89-3P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of N3-substituted 6-anilinopyrimidines to treat Gram-pos. bacterial and mycoplasmal infections)
RN 478921-24-3 CAPLUS
CN 1(2H)-Pyrimidinepentanoic acid, 4-[(3-ethyl-4-methylphenyl)amino]-3,6-dihydro-2,6-dioxo-, ethyl ester (9CI) (CA INDEX NAME)

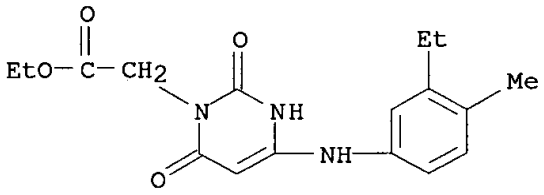


RN 480446-12-6 CAPLUS
CN 1(2H)-Pyrimidinebutanoic acid, 4-[(3-ethyl-4-methylphenyl)amino]-3,6-

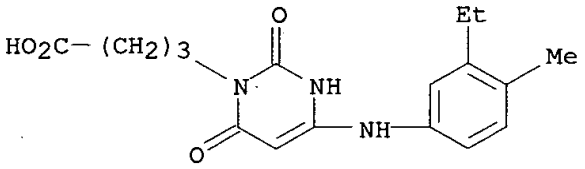
dihydro-2,6-dioxo-, ethyl ester (9CI) (CA INDEX NAME)



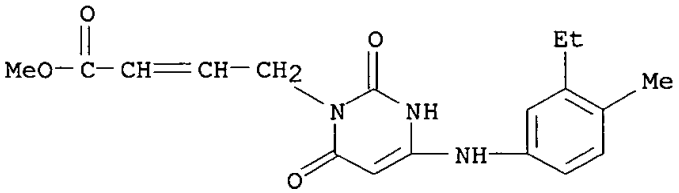
RN 496942-89-3 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 4-[(3-ethyl-4-methylphenyl)amino]-3,6-dihydro-2,6-dioxo-, ethyl ester (9CI) (CA INDEX NAME)



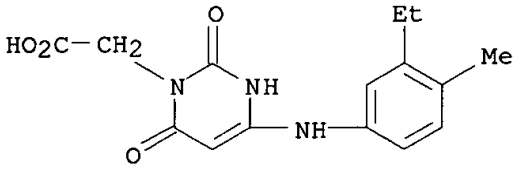
IT **480446-16-0P 496942-85-9P 496942-99-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N3-substituted 6-anilinopyrimidines to treat Gram-pos. bacterial and mycoplasmal infections)
RN 480446-16-0 CAPLUS
CN 1(2H)-Pyrimidinebutanoic acid, 4-[(3-ethyl-4-methylphenyl)amino]-3,6-dihydro-2,6-dioxo- (9CI) (CA INDEX NAME)



RN 496942-85-9 CAPLUS
CN 2-Butenoic acid, 4-[4-[(3-ethyl-4-methylphenyl)amino]-3,6-dihydro-2,6-dioxo-1(2H)-pyrimidinyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 496942-99-5 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 4-[(3-ethyl-4-methylphenyl)amino]-3,6-dihydro-2,6-dioxo- (9CI) (CA INDEX NAME)



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

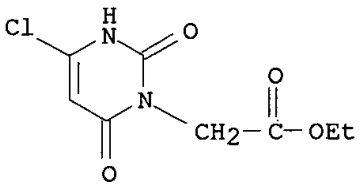
L8 ANSWER 2 OF 212 CAPLUS COPYRIGHT 2003 ACS
AN 2003:5936 CAPLUS
DN 138:73264
TI Preparation of 6-anilinouracils as DNA polymerase III inhibitors for the treatment of bacterial diseases
IN Flubacher, Dietmar; Ehlert, Kerstin; Kuhl, Alexander; Svenstrup, Niels; Bauser, Marcus; Keldenich, Joerg; Otteneder, Michael; Ladel, Christoph
PA Bayer Aktiengesellschaft, Germany
SO PCT Int. Appl., 108 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003000665	A1	20030103	WO 2002-EP6325	20020610

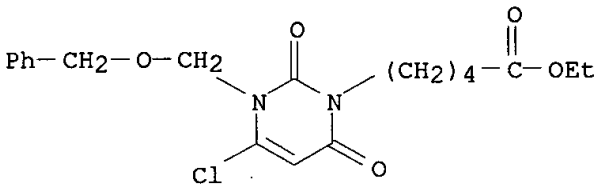
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI DE 2001-10130149 A 20010622
DE 2002-10200485 A 20020109
OS MARPAT 138:73264
AB Title compd. I [R1 and R2 together with the nitrogen atom form a heterocyclic ring;R3, R4 = alkyl, alkenyl, alkynyl, etc.; A =C1-C6alkylene, which if necessary contains double or triple bonds, with provisos] were prepd. For example, coupling of carboxylic acid II, prepd. in 3-steps from (2,4,6-trioxotetrahydro-1(2H)-pyrimidinyl)acetic acid Et ester, and 1-phenylpiperazine provided anilinouracil III in 59% yield. In DNA Polymerase III inhibition assays, 6-specific examples of compds. I exhibited IC50 values in the range of 0.15-2.07 .mu.M. Compds. I are useful for the treatment of bacterial diseases affecting humans or animals.
IT **98629-85-7P**, (4-Chloro-2,6-dioxo-3,6-dihydro-1(2H)-pyrimidinyl)acetic acid ethyl ester **480446-06-8P**, 5-[3-[(Benzyloxy)methyl]-4-chloro-2,6-dioxo-3,6-dihydro-1(2H)-pyrimidinyl]pentanoic acid ethyl ester **480446-07-9P**, 5-(4-Chloro-2,6-dioxo-3,6-dihydro-1(2H)-pyrimidinyl)pentanoic acid ethyl ester **480446-08-0P**, 4-[4-(2,3-Dihydro-1H-inden-5-ylamino)-2,6-dioxo-3,6-dihydro-1(2H)-pyrimidinyl]butanoic acid ethyl ester **480446-10-4P**, [4-(2,3-Dihydro-1H-inden-5-ylamino)-2,6-dioxo-3,6-dihydro-1(2H)-pyrimidinyl]acetic acid ethyl ester **480446-11-5P**, 4-[4-[(3-Chloro-4-methylphenyl)amino]-2,6-dioxo-3,6-dihydro-1(2H)-pyrimidinyl]butanoic acid ethyl ester **480446-12-6P**, 4-[4-[(3-Ethyl-4-methylphenyl)amino]-2,6-dioxo-3,6-dihydro-1(2H)-pyrimidinyl]butanoic acid ethyl ester **480446-14-8P**, 4-[4-(2,3-Dihydro-1H-inden-5-ylamino)-2,6-dioxo-3,6-dihydro-1(2H)-pyrimidinyl]butanoic acid
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of anilinouracils as DNA Polymerase III inhibitors for the treatment of bacterial diseases)

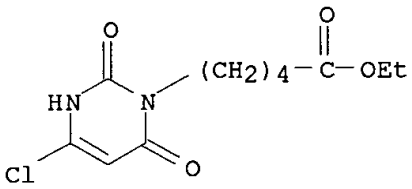
RN 98629-85-7 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 4-chloro-3,6-dihydro-2,6-dioxo-, ethyl ester (9CI) (CA INDEX NAME)



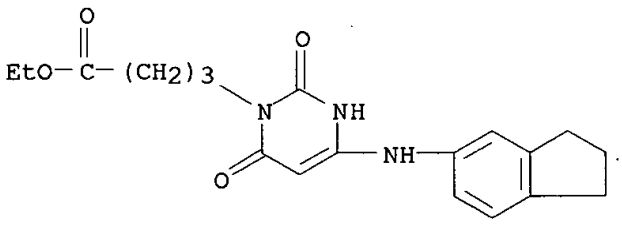
RN 480446-06-8 CAPLUS
CN 1(2H)-Pyrimidinepentanoic acid, 4-chloro-3,6-dihydro-2,6-dioxo-3-[(phenylmethoxy)methyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 480446-07-9 CAPLUS
CN 1(2H)-Pyrimidinepentanoic acid, 4-chloro-3,6-dihydro-2,6-dioxo-, ethyl ester (9CI) (CA INDEX NAME)

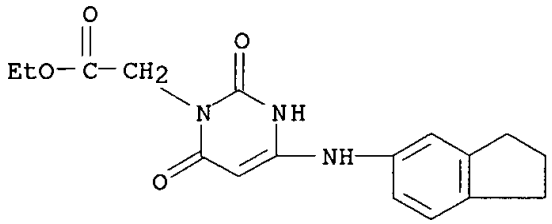


RN 480446-08-0 CAPLUS
CN 1(2H)-Pyrimidinebutanoic acid, 4-[(2,3-dihydro-1H-inden-5-yl)amino]-3,6-dihydro-2,6-dioxo-, ethyl ester (9CI) (CA INDEX NAME)

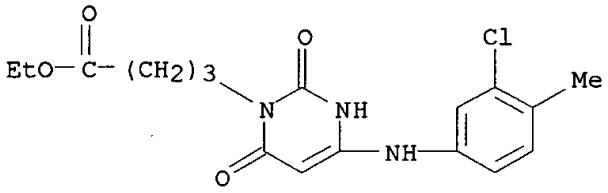


RN 480446-10-4 CAPLUS

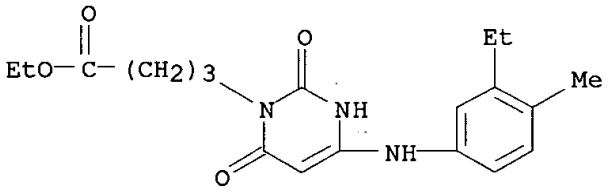
CN 1(2H)-Pyrimidineacetic acid, 4-[(2,3-dihydro-1H-inden-5-yl)amino]-3,6-dihydro-2,6-dioxo-, ethyl ester (9CI) (CA INDEX NAME)



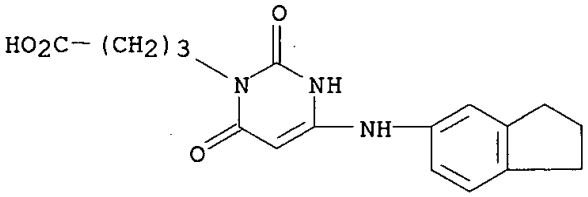
RN 480446-11-5 CAPLUS
CN 1(2H)-Pyrimidinebutanoic acid, 4-[(3-chloro-4-methylphenyl)amino]-3,6-dihydro-2,6-dioxo-, ethyl ester (9CI) (CA INDEX NAME)



RN 480446-12-6 CAPLUS
CN 1(2H)-Pyrimidinebutanoic acid, 4-[(3-ethyl-4-methylphenyl)amino]-3,6-dihydro-2,6-dioxo-, ethyl ester (9CI) (CA INDEX NAME)



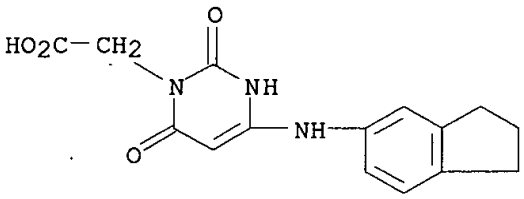
RN 480446-14-8 CAPLUS
CN 1(2H)-Pyrimidinebutanoic acid, 4-[(2,3-dihydro-1H-inden-5-yl)amino]-3,6-dihydro-2,6-dioxo- (9CI) (CA INDEX NAME)



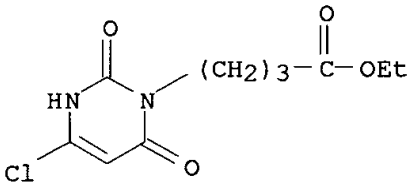
IT **177792-96-0**, [4-(2,3-Dihydro-1H-inden-5-ylamino)-2,6-dioxo-3,6-dihydro-1(2H)-pyrimidinyl]acetic acid **480446-09-1**,

4-(4-Chloro-2,6-dioxo-3,6-dihydro-1(2H)-pyrimidinyl)butanoic acid ethyl ester **480446-13-7**, 5-[4-(2,3-Dihydro-1H-inden-5-ylamino)-2,6-dioxo-3,6-dihydro-1(2H)-pyrimidinyl]pentanoic acid ethyl ester **480446-16-0**, 4-[4-[(3-Ethyl-4-methylphenyl)amino]-2,6-dioxo-3,6-dihydro-1(2H)-pyrimidinyl]butanoic acid **480446-17-1**, 5-[4-(2,3-Dihydro-1H-inden-5-ylamino)-2,6-dioxo-3,6-dihydro-1(2H)-pyrimidinyl]pentanoic acid **481724-79-2**, 4-[4-[(3-Chloro-4-methylphenyl)amino]-2,6-dioxo-3,6-dihydro-1(2H)-pyrimidinyl]butanooic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of anilinouracils as DNA Polymerase III inhibitors for the treatment of bacterial diseases)

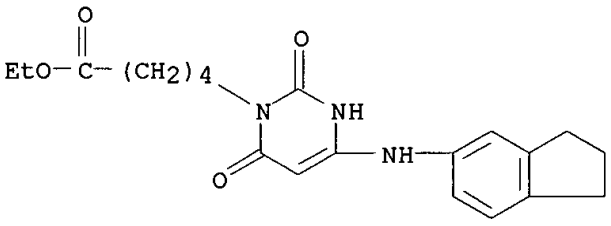
RN 177792-96-0 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 4-[(2,3-dihydro-1H-inden-5-yl)amino]-3,6-dihydro-2,6-dioxo- (9CI) (CA INDEX NAME)



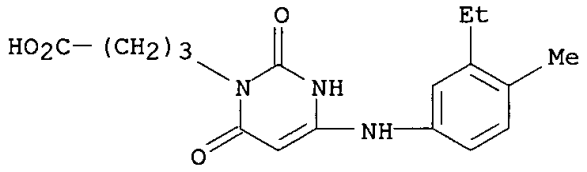
RN 480446-09-1 CAPLUS
CN 1(2H)-Pyrimidinebutanoic acid, 4-chloro-3,6-dihydro-2,6-dioxo-, ethyl ester (9CI) (CA INDEX NAME)



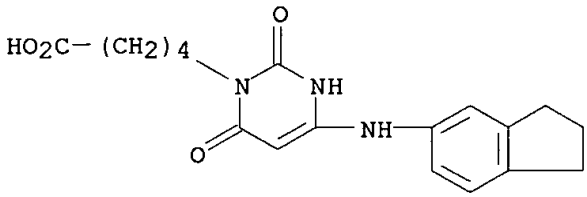
RN 480446-13-7 CAPLUS
CN 1(2H)-Pyrimidinepentanoic acid, 4-[(2,3-dihydro-1H-inden-5-yl)amino]-3,6-dihydro-2,6-dioxo-, ethyl ester (9CI) (CA INDEX NAME)



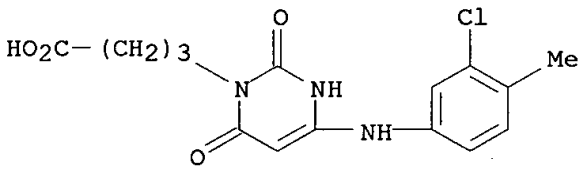
RN 480446-16-0 CAPLUS
CN 1(2H)-Pyrimidinebutanoic acid, 4-[(3-ethyl-4-methylphenyl)amino]-3,6-dihydro-2,6-dioxo- (9CI) (CA INDEX NAME)



RN 480446-17-1 CAPLUS
CN 1(2H)-Pyrimidinepentanoic acid, 4-[(2,3-dihydro-1H-inden-5-yl)amino]-3,6-dihydro-2,6-dioxo- (9CI) (CA INDEX NAME)



RN 481724-79-2 CAPLUS
CN 1(2H)-Pyrimidinebutanoic acid, 4-[(3-chloro-4-methylphenyl)amino]-3,6-dihydro-2,6-dioxo- (9CI) (CA INDEX NAME)



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

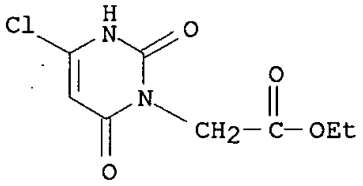
L8 ANSWER 3 OF 212 CAPLUS COPYRIGHT 2003 ACS
AN 2003:5935 CAPLUS
DN 138:73263
TI Preparation of 6-anilinouracils as DNA polymerase III inhibitors for the treatment of bacterial diseases
IN Flubacher, Dietmar; Ehlert, Kerstin; Kuhl, Alexander; Svenstrup, Niels; Bauser, Marcus; Keldenich, Joerg; Otteneder, Michael
PA Bayer Aktiengesellschaft, Germany
SO PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003000664	A1	20030103	WO 2002-EP6311	20020610

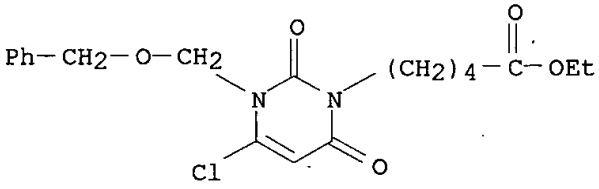
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI DE 2001-10130148 A 20010622
DE 2001-10162744 A 20011220
OS MARPAT 138:73263
AB Title compd. I [R1 = cycloalkyl, aryl, heterocycle, etc.; R2 = H, alkyl, cycloalkyl, etc.; R3, R4 = alkyl, alkenyl, alkynyl, etc.; A, E = C1-C6alkylene, which if necessary contains double or triple bonds with provisos] and their pharmaceutically acceptable salts were prepd. For example, coupling of carboxylic acid II, prepd. in 6-steps from 6-chloro-2,4(1H,3H)-pyrimidinedione, and benzylamine provided aminouracil III in 6% yield. In DNA Polymerase III inhibition assays, 6-specific examples of compds. I exhibited IC50 values ranging from 0.21-1.0 .mu.M. Compds. I are useful for the treatment of bacterial diseases affecting humans or animals.
IT **98629-85-7P**, (4-Chloro-2,6-dioxo-3,6-dihydro-1(2H)-pyrimidinyl)acetic acid ethyl ester **480446-06-8P**, 5-[3-[(Benzyloxy)methyl]-4-chloro-2,6-dioxo-3,6-dihydro-1(2H)-pyrimidinyl]pentanoic acid ethyl ester **480446-07-9P**, 5-(4-Chloro-2,6-dioxo-3,6-dihydro-1(2H)-pyrimidinyl)pentanoic acid ethyl ester **480446-08-0P**, 4-[4-(2,3-Dihydro-1H-inden-5-ylamino)-2,6-dioxo-3,6-dihydro-1(2H)-pyrimidinyl]butanoic acid ethyl ester **480446-10-4P**, [4-(2,3-Dihydro-1H-inden-5-ylamino)-2,6-dioxo-3,6-dihydro-1(2H)-pyrimidinyl]acetic acid ethyl ester **480446-11-5P**, 4-[4-[(3-Chloro-4-methylphenyl)amino]-2,6-dioxo-3,6-dihydro-1(2H)-pyrimidinyl]butanoic acid ethyl ester **480446-12-6P**, 4-[4-[(3-Ethyl-4-methylphenyl)amino]-2,6-dioxo-3,6-dihydro-1(2H)-pyrimidinyl]butanoic acid ethyl ester **480446-14-8P**, 4-[4-(2,3-Dihydro-1H-inden-5-ylamino)-2,6-dioxo-3,6-dihydro-1(2H)-pyrimidinyl]butanoic acid
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of aminouracils as DNA Polymerase III inhibitors for the treatment of bacterial diseases)

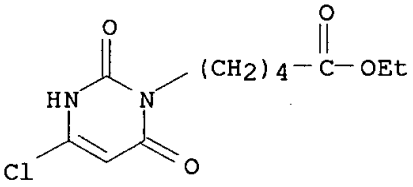
RN 98629-85-7 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 4-chloro-3,6-dihydro-2,6-dioxo-, ethyl ester (9CI) (CA INDEX NAME)



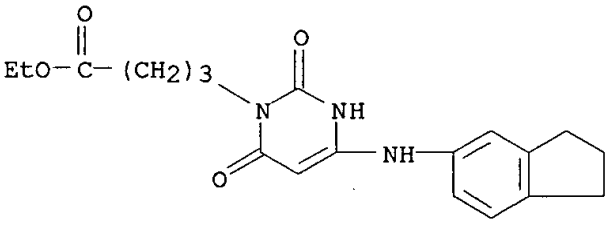
RN 480446-06-8 CAPLUS
CN 1(2H)-Pyrimidinepentanoic acid, 4-chloro-3,6-dihydro-2,6-dioxo-3-[(phenylmethoxy)methyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 480446-07-9 CAPLUS
CN 1(2H)-Pyrimidinepentanoic acid, 4-chloro-3,6-dihydro-2,6-dioxo-, ethyl ester (9CI) (CA INDEX NAME)

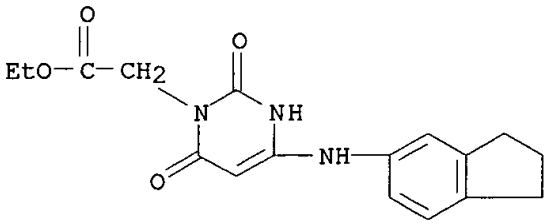


RN 480446-08-0 CAPLUS
CN 1(2H)-Pyrimidinebutanoic acid, 4-[(2,3-dihydro-1H-inden-5-yl)amino]-3,6-dihydro-2,6-dioxo-, ethyl ester (9CI) (CA INDEX NAME)

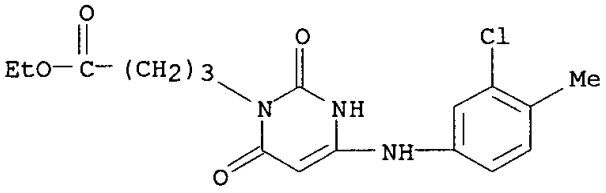


RN 480446-10-4 CAPLUS

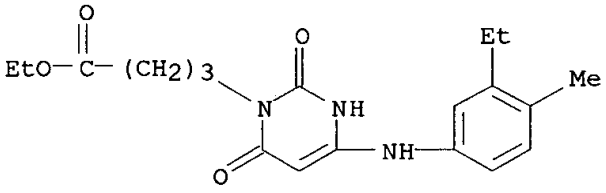
CN 1(2H)-Pyrimidineacetic acid, 4-[(2,3-dihydro-1H-inden-5-yl)amino]-3,6-dihydro-2,6-dioxo-, ethyl ester (9CI) (CA INDEX NAME)



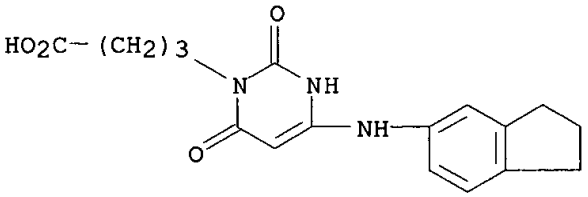
RN 480446-11-5 CAPLUS
CN 1(2H)-Pyrimidinebutanoic acid, 4-[(3-chloro-4-methylphenyl)amino]-3,6-dihydro-2,6-dioxo-, ethyl ester (9CI) (CA INDEX NAME)



RN 480446-12-6 CAPLUS
CN 1(2H)-Pyrimidinebutanoic acid, 4-[(3-ethyl-4-methylphenyl)amino]-3,6-dihydro-2,6-dioxo-, ethyl ester (9CI) (CA INDEX NAME)



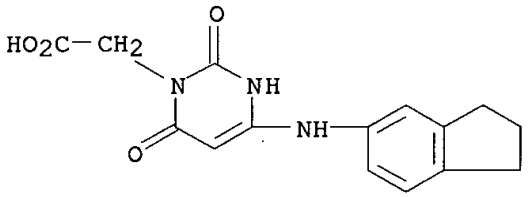
RN 480446-14-8 CAPLUS
CN 1(2H)-Pyrimidinebutanoic acid, 4-[(2,3-dihydro-1H-inden-5-yl)amino]-3,6-dihydro-2,6-dioxo- (9CI) (CA INDEX NAME)



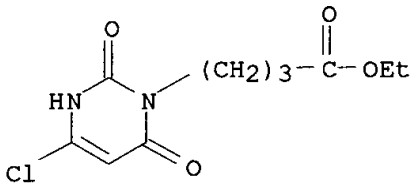
IT **177792-96-0**, [4-(2,3-Dihydro-1H-inden-5-ylamino)-2,6-dioxo-3,6-dihydro-1(2H)-pyrimidinyl]acetic acid **480446-09-1**,

4-(4-Chloro-2,6-dioxo-3,6-dihydro-1(2H)-pyrimidinyl)butanoic acid ethyl ester **480446-13-7**, 5-[4-(2,3-Dihydro-1H-inden-5-ylamino)-2,6-dioxo-3,6-dihydro-1(2H)-pyrimidinyl]pentanoic acid ethyl ester **480446-15-9**, 4-[4-[(3-Chloro-methylphenyl)amino]-2,6-dioxo-3,6-dihydro-1(2H)-pyrimidinyl]butanoic acid **480446-16-0**, 4-[4-[(3-Ethyl-4-methylphenyl)amino]-2,6-dioxo-3,6-dihydro-1(2H)-pyrimidinyl]butanoic acid **480446-17-1**, 5-[4-(2,3-Dihydro-1H-inden-5-ylamino)-2,6-dioxo-3,6-dihydro-1(2H)-pyrimidinyl]pentanoic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of aminouracils as DNA Polymerase III inhibitors for the treatment of bacterial diseases)

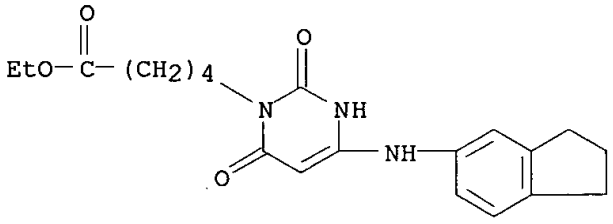
RN 177792-96-0 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 4-[(2,3-dihydro-1H-inden-5-yl)amino]-3,6-dihydro-2,6-dioxo- (9CI) (CA INDEX NAME)



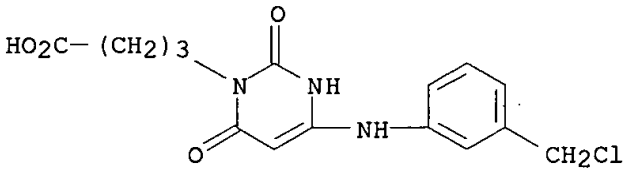
RN 480446-09-1 CAPLUS
CN 1(2H)-Pyrimidinebutanoic acid, 4-chloro-3,6-dihydro-2,6-dioxo-, ethyl ester (9CI) (CA INDEX NAME)



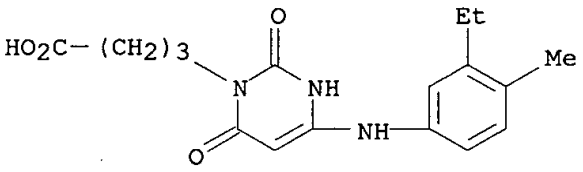
RN 480446-13-7 CAPLUS
CN 1(2H)-Pyrimidinepentanoic acid, 4-[(2,3-dihydro-1H-inden-5-yl)amino]-3,6-dihydro-2,6-dioxo-, ethyl ester (9CI) (CA INDEX NAME)



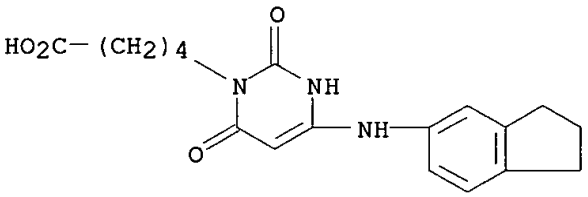
RN 480446-15-9 CAPLUS
CN 1(2H)-Pyrimidinebutanoic acid, 4-[[3-(chloromethyl)phenyl]amino]-3,6-dihydro-2,6-dioxo- (9CI) (CA INDEX NAME)



RN 480446-16-0 CAPLUS
CN 1(2H)-Pyrimidinebutanoic acid, 4-[(3-ethyl-4-methylphenyl)amino]-3,6-dihydro-2,6-dioxo- (9CI) (CA INDEX NAME)



RN 480446-17-1 CAPLUS
CN 1(2H)-Pyrimidinepentanoic acid, 4-[(2,3-dihydro-1H-inden-5-yl)amino]-3,6-dihydro-2,6-dioxo- (9CI) (CA INDEX NAME)



RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

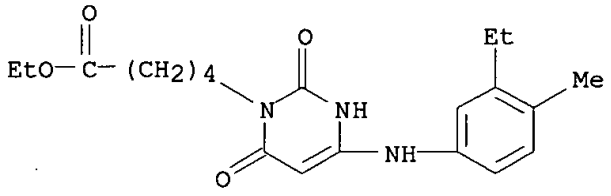
L8 ANSWER 4 OF 212 CAPLUS COPYRIGHT 2003 ACS
AN 2002:977783 CAPLUS
DN 138:39292
TI Methods for synthesizing N3-substituted pyrimidones
IN Zhi, Chengxin; Long, Zheng-Yu; Wright, George E.; Manikowski, Andrzej
PA University of Massachusetts, USA
SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002102769	A2	20021227	WO 2002-US19399	20020617

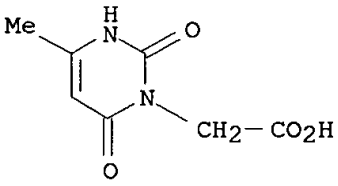
PI
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-298436P P 20010615
OS CASREACT 138:39292
AB A method of prepg. a 6-amino-2-alkoxy-3-substituted-4-pyrimidone by combining a 4-pyrimidone and a nonaq. base, followed by an alkylating agent is disclosed. This method has the advantages of resulting in preferential synthesis of the N3-isomer rather than the O4-isomer and working even when the starting 4-pyrimidone contains a sensitive functional group. A method of prepg. a N3-alkyl-6-(substituted amino)uracil is also disclosed. The method includes (a) combining an N3-substituted-2-alkoxy-6-amino-4-pyrimidone with an amine compd. selected from the group consisting of an amine salt and the corresponding free amine, to form a reaction mixt.; and (b) heating the reaction mixt. to at least 80.degree. for a time sufficient for the N3-substituted-2-alkoxy-6-amino-4-pyrimidone and the amine compd. to react to form the final product. This method offers the advantages of using mild reaction conditions, accomplishing both 6-substitution and 2-dealkylation in a one-pot reaction, reacting in the absence of a solvent, and running at high temps., which shortens the reaction times. For example, addn. of LiBr to a mixt. of 6-amino-2-methoxy-4-pyrimidone and NaH in DMF and stirring at room temp. for 1 h, followed by addn. of 4-bromo-1-acetoxybutane in DMF at 50.degree. afforded 6-amino-2-methoxy-3-(4-acetoxybutyl)pyrimidin-4(3H)-one (54%) and the O4-isomer (35%). The pyrimidinone mixt. was heated with 3-ethyl-4-methylaniline.bul.HCl and 3-ethyl-4-methylaniline in an oil bath at 160.degree. for 15 min and worked up to give 3-(4-acetoxybutyl)-6-(3-ethyl-4-methylanilino)uracil (84%).
IT **478921-24-3P**, 3-(4-Ethoxycarbonylbutyl)-6-(3-ethyl-4-methylanilino)uracil
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of N3-substituted 6-(substituted amino)uracils by reaction of N3-substituted-6-aminopyrimidones with amines)
RN 478921-24-3 CAPLUS
CN 1(2H)-Pyrimidinepentanoic acid, 4-[(3-ethyl-4-methylphenyl)amino]-3,6-

dihydro-2,6-dioxo-, ethyl ester (9CI) (CA INDEX NAME)



L8 ANSWER 5 OF 212 CAPLUS COPYRIGHT 2003 ACS
AN 2002:725916 CAPLUS
TI (6-Methyl-2-methylsulfanyl-4-oxo-3,4-dihydro-3-pyrimidinyl)acetic acid and related compounds exhibiting anti-inflammatory activity
AU Jakubkiene, V.; Burbuliene, M. M.; Udrenaite, E.; Garaliene, V.; Vainilavicius, P.
CS Fac. of Chemistry, Vilnius Univ., Lithuania
SO Pharmazie (2002), 57(9), 610-613
CODEN: PHARAT; ISSN: 0031-7144
PB Govi-Verlag Pharmazeutischer Verlag GmbH
DT Journal
LA English
AB Base-promoted hydrolysis of Me or Et esters 1a-c gave the (6-methyl-2-methylsulfanyl-4-oxo-3,4-dihydro-3-pyrimidinyl)- and (5-ethyl-6-methyl-2-methylsulfanyl-4-oxo-3,4-dihydro-3-pyrimidinyl)acetic acids 2a, b. Under the reaction of ester 1a or acid 2a with nucleophilic reagents a series of derivs. 3-7 of acid 2a were synthesized and evaluated for their anti-inflammatory activity. Most of them were found to be more active than acetylsalicylic acid, and compds. 2a, 6a, b, 7a, f were significantly more active than ibuprofen. The compds. exhibiting the best anti-inflammatory activity showed neg. inotropic effect.
IT **54069-85-1**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of (6-Me-2-methylsulfanyl-4-oxo-3,4-dihydro-3-pyrimidinyl)acetic acid and related compds. and their anti-inflammatory and neg. inotropic activity)
RN 54069-85-1 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 3,6-dihydro-4-methyl-2,6-dioxo- (9CI) (CA INDEX NAME)



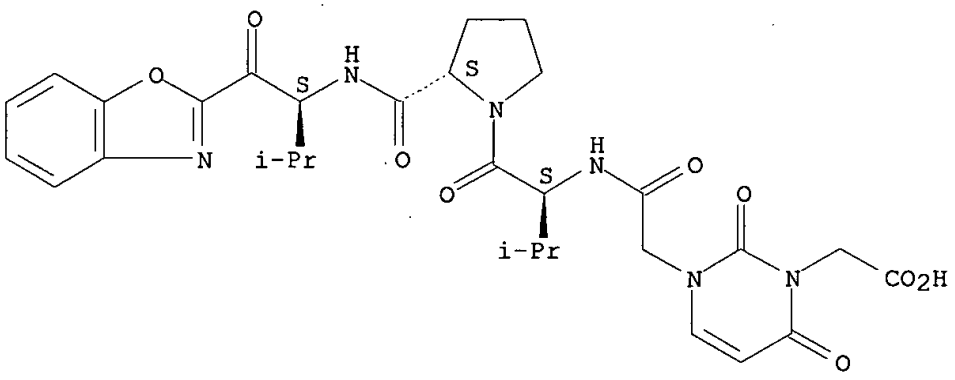
RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 212 CAPLUS COPYRIGHT 2003 ACS
AN 2002:359856 CAPLUS
DN 136:369997
TI Pharmaceuticals containing heterocyclyl group-containing prolines as water-soluble inhibitors of human neutrophil elastase
IN Sato, Fuminori; Inoue, Yasuharu; Omotani, Tomoki; Shiratake, Ryotaro; Honda, Seiji; Komiya, Masanobu; Takemura, Tadashi
PA Dainippon Pharmaceutical Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 41 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2002138048	A2	20020514	JP 2001-251265	20010822
PRAI JP 2000-254746	A	20000825		

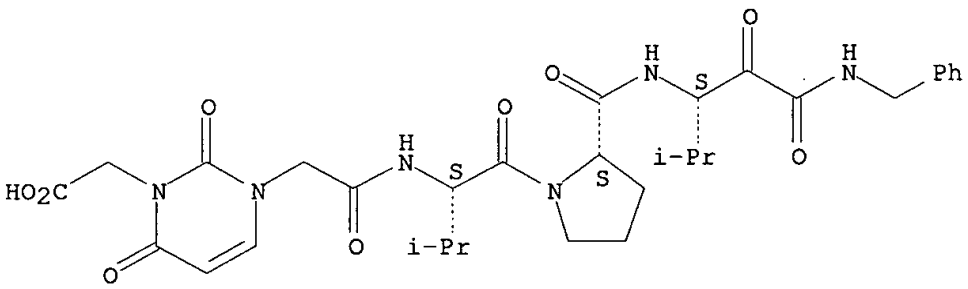
OS MARPAT 136:369997
AB Title compds. I [A, B = (oxo-substituted) lower alkylene D = Q; D1 = (oxo-substituted) CH2, (oxo-substituted) CH2CH2; the ring G = 5- to 14-membered monocyclic (un)satd. (un)substituted heterocycle reside (having addnl. N, O, and/or S); R1, R2 = lower alkyl; R3 = (CX1X2)n(CH2)mY1; X1, X2 = halo; Y1 = H, halo, lower alkoxycarbonyl, lower alkylaminocarbonyl, etc.] or their physiol. acceptable salts are prepd. and are esp. useful for therapeutic and prophylactic treatment of acute lung disease, e.g. emphysema and acute respiratory distress syndrome. Thus, condensation of 2-[(3-tert-butoxycarbonylmethyl-2-oxo-1-imidazolidinyl)]acetic acid with L-valyl-N-[(1S,2S)-(3,3,3-trifluoro-1-isopropyl-2-hydroxypropyl)]-L-prolinamide HCl salt gave the corresponding amide, which was oxidized with Dess-Martin reagent and deprotected to afford 2-(3-carboxymethyl-2-oxo-1-imidazolidinyl)acetyl-L-valyl-N-[(1S)-3,3,3-trifluoro-1-isopropyl-2-oxopropyl]-L-prolinamide. The product inhibited human neutrophil elastase at IC50 value of 0.010 .mu.M and showed much better water soly. than ONO-5046.
IT **291778-79-5P 291778-80-8P**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of heterocyclyl group-contg. prolines as water-sol. inhibitors of human neutrophil elastase)
RN 291778-79-5 CAPLUS
CN L-Prolinamide, N-[[3-(carboxymethyl)-3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl]acetyl]-L-valyl-N-[(1S)-1-(2-benzoxazolylcarbonyl)-2-methylpropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



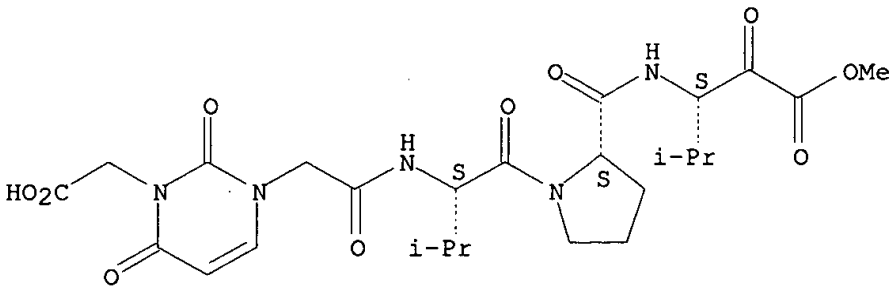
RN 291778-80-8 CAPLUS
CN L-Prolinamide, N-[[3-(carboxymethyl)-3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl]acetyl]-L-valyl-N-[(1S)-1-(1-methylethyl)-2,3-dioxo-3-[(phenylmethyl)amino]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



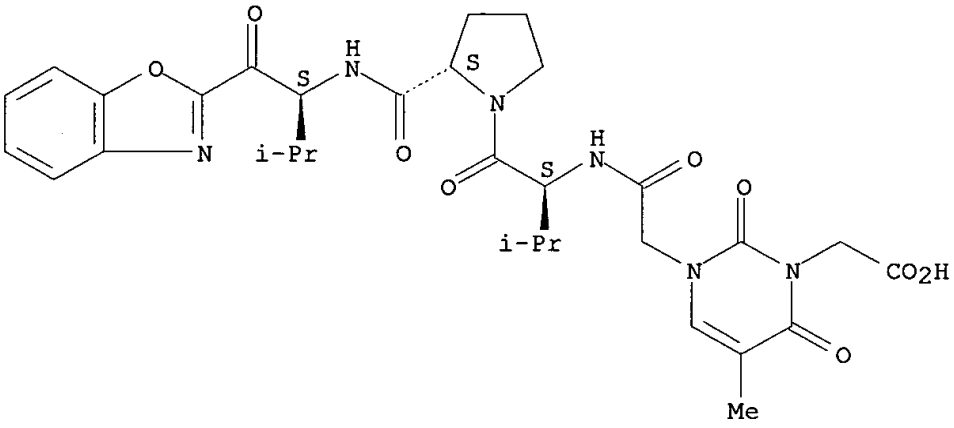
IT **291778-95-5P 291779-03-8P 291779-19-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of heterocyclyl group-contg. prolines as water-sol. inhibitors of human neutrophil elastase)
RN 291778-95-5 CAPLUS
CN L-Prolinamide, N-[[3-(carboxymethyl)-3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl]acetyl]-L-valyl-N-[(1S)-3-methoxy-1-(1-methylethyl)-2,3-dioxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



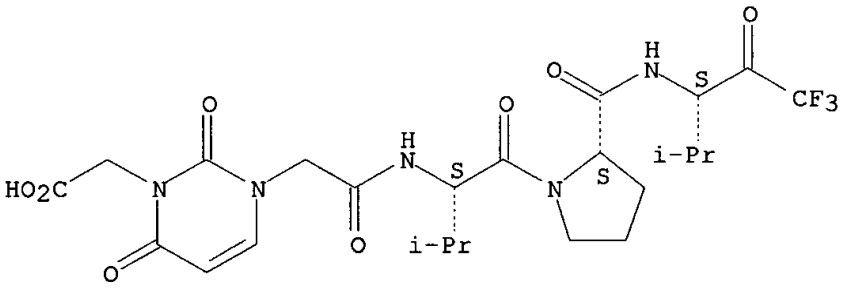
RN 291779-03-8 CAPLUS
CN L-Prolinamide, N-[[3-(carboxymethyl)-3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl]acetyl]-L-valyl-N-[(1S)-1-(2-benzoxazolylcarbonyl)-2-methylpropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 291779-19-6 CAPLUS
CN L-Prolinamide, N-[[3-(carboxymethyl)-3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl]acetyl]-L-valyl-N-[(1S)-3,3,3-trifluoro-1-(1-methylethyl)-2-oxopropyl]- (9CI) (CA INDEX NAME)

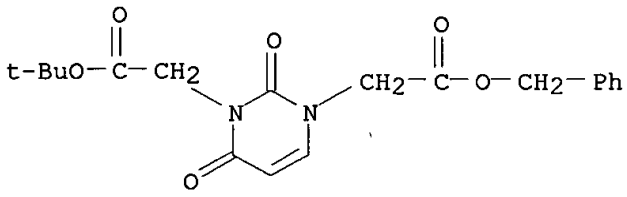
Absolute stereochemistry.



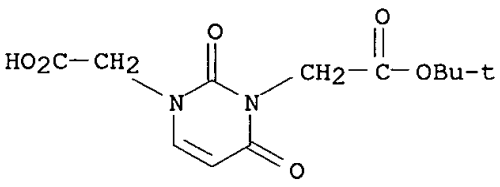
IT **291778-28-4P 291778-30-8P 291778-37-5P**
291778-38-6P 291778-41-1P 291778-53-5P

291778-54-6P 291778-60-4P 291778-64-8P
291778-78-4P 423118-68-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of heterocyclyl group-contg. prolines as water-sol. inhibitors of human neutrophil elastase)

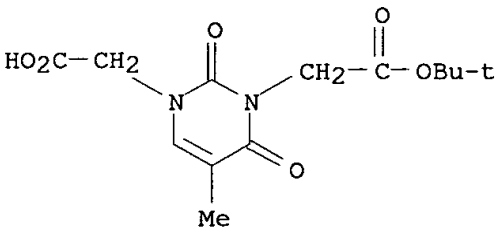
RN 291778-28-4 CAPLUS
CN 1,3(2H,4H)-Pyrimidinediacetic acid, 2,4-dioxo-, .alpha.3-(1,1-dimethylethyl) .alpha.1-(phenylmethyl) ester (9CI) (CA INDEX NAME)



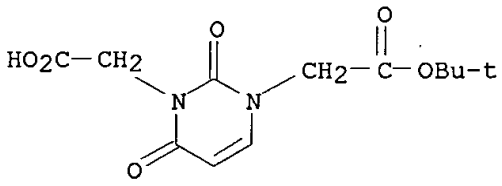
RN 291778-30-8 CAPLUS
CN 1,3(2H,4H)-Pyrimidinediacetic acid, 2,4-dioxo-, .alpha.3-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



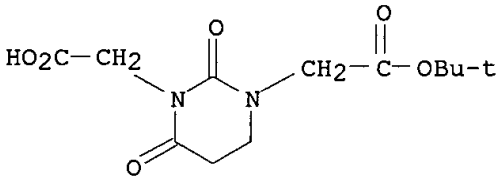
RN 291778-37-5 CAPLUS
CN 1,3(2H,4H)-Pyrimidinediacetic acid, 5-methyl-2,4-dioxo-, .alpha.3-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



RN 291778-38-6 CAPLUS
CN 1,3(2H,4H)-Pyrimidinediacetic acid, 2,4-dioxo-, .alpha.1-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

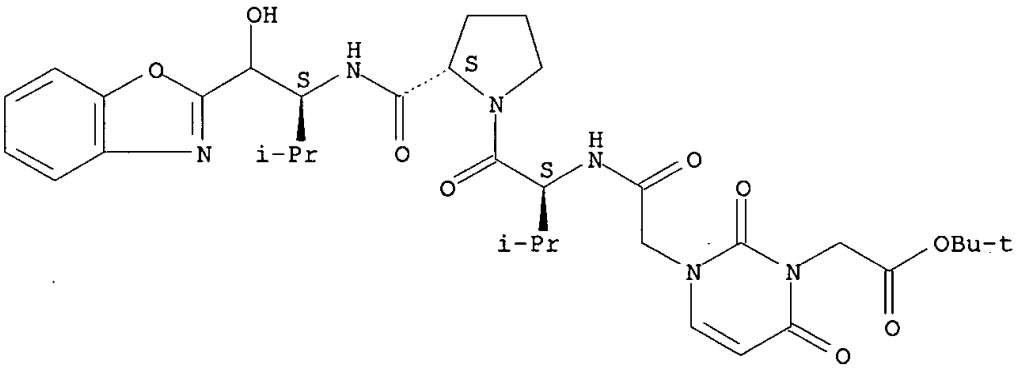


RN 291778-41-1 CAPLUS
CN 1,3(2H,4H)-Pyrimidinediacetic acid, dihydro-2,4-dioxo-, .alpha.1-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



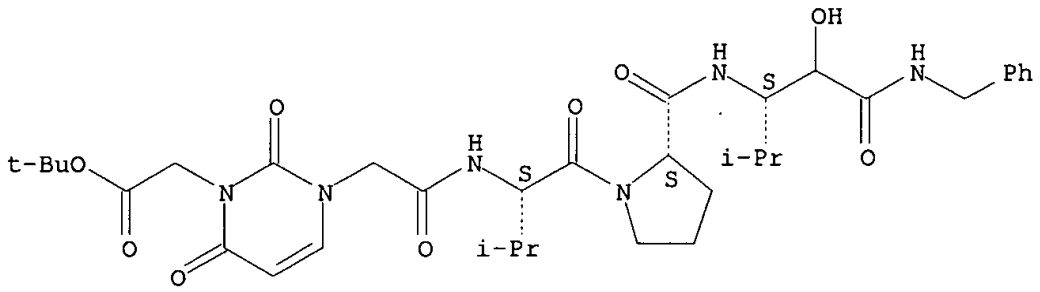
RN 291778-53-5 CAPLUS
CN L-Prolinamide, N-[[3-[2-(1,1-dimethylethoxy)-2-oxoethyl]-3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl]acetyl]-L-valyl-N-[(1S)-1-(2-benzoxazolylhydroxymethyl)-2-methylpropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



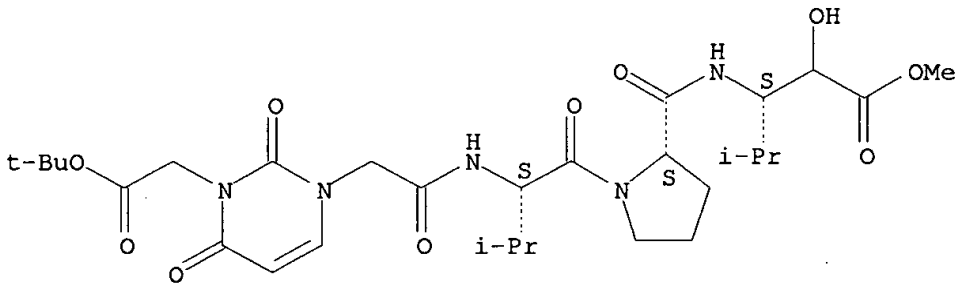
RN 291778-54-6 CAPLUS
CN L-glycero-Pentonamide, 3,4,5-trideoxy-3-[[N-[[3-[2-(1,1-dimethylethoxy)-2-oxoethyl]-3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl]acetyl]-L-valyl-L-prolyl]amino]-4-methyl-N-(phenylmethyl)-, (2.xi.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



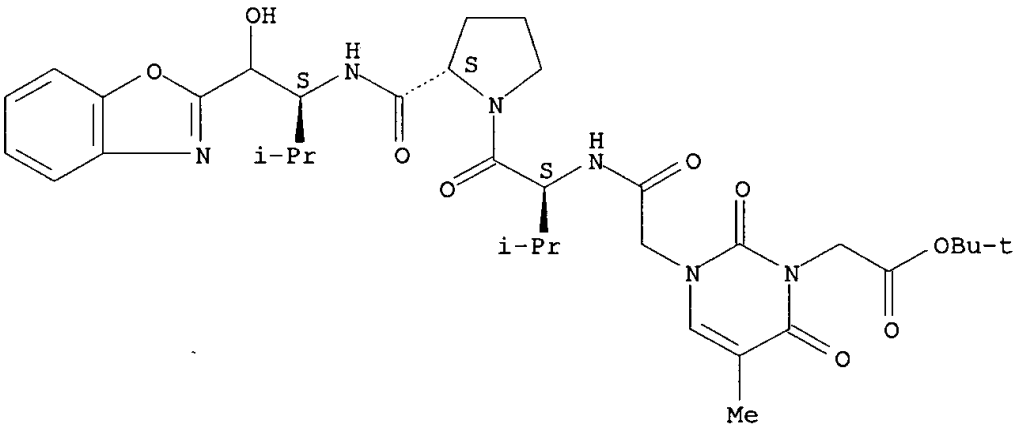
RN 291778-60-4 CAPLUS
CN L-glycero-Pentonic acid, 3,4,5-trideoxy-3-[[N-[[3-[2-(1,1-dimethylethoxy)-2-oxoethyl]-3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl]acetyl]-L-valyl-L-prolyl]amino]-4-methyl-, methyl ester, (2.xi.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 291778-64-8 CAPLUS
CN L-Prolinamide, N-[[3-[2-(1,1-dimethylethoxy)-2-oxoethyl]-3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl]acetyl]-L-valyl-N-[(1S)-1-(2-benzoxazolylhydroxymethyl)-2-methylpropyl]- (9CI) (CA INDEX NAME)

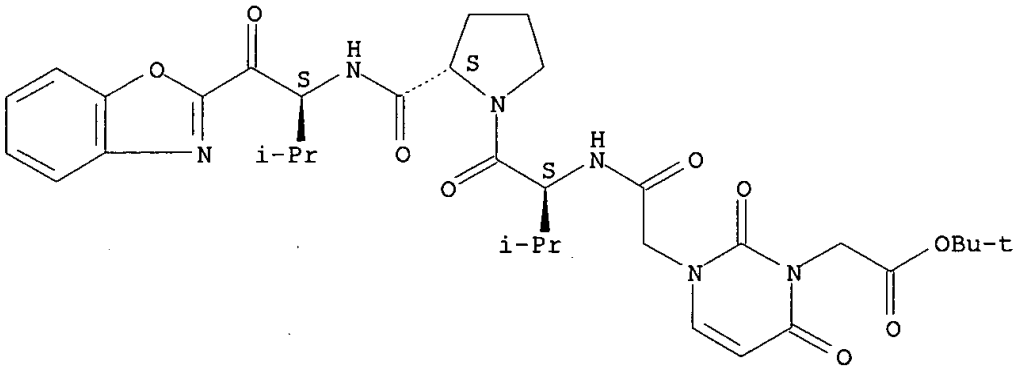
Absolute stereochemistry.



RN 291778-78-4 CAPLUS
CN L-Prolinamide, N-[[3-[2-(1,1-dimethylethoxy)-2-oxoethyl]-3,4-dihydro-2,4-

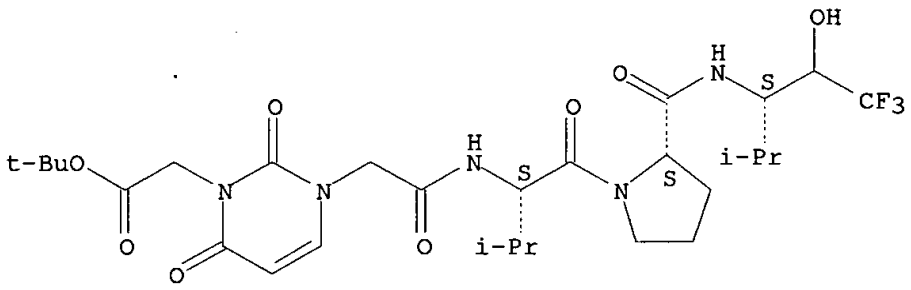
dioxo-1(2H)-pyrimidinyl]acetyl]-L-valyl-N-[(1S)-1-(2-benzoxazolylcarbonyl)-2-methylpropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



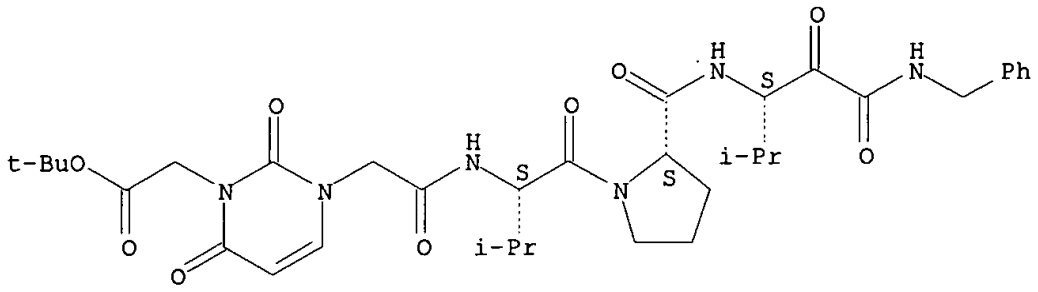
RN 423118-68-7 CAPLUS
CN L-Prolinamide, N-[[3-[2-(1,1-dimethylethoxy)-2-oxoethyl]-3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl]acetyl]-L-valyl-N-[(1S)-3,3,3-trifluoro-2-hydroxy-1-(1-methylethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



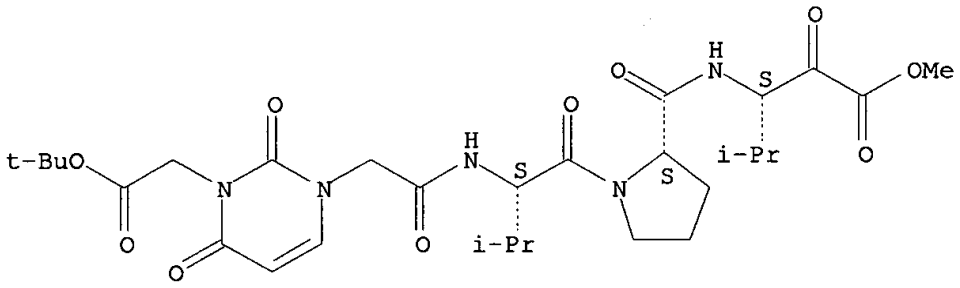
IT **291778-81-9P 291778-96-6P 291779-04-9P 291779-20-9P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of heterocyclyl group-contg. prolines as water-sol. inhibitors of human neutrophil elastase)
RN 291778-81-9 CAPLUS
CN L-Prolinamide, N-[[3-[2-(1,1-dimethylethoxy)-2-oxoethyl]-3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl]acetyl]-L-valyl-N-[(1S)-1-(1-methylethyl)-2,3-dioxo-3-[(phenylmethyl)amino]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



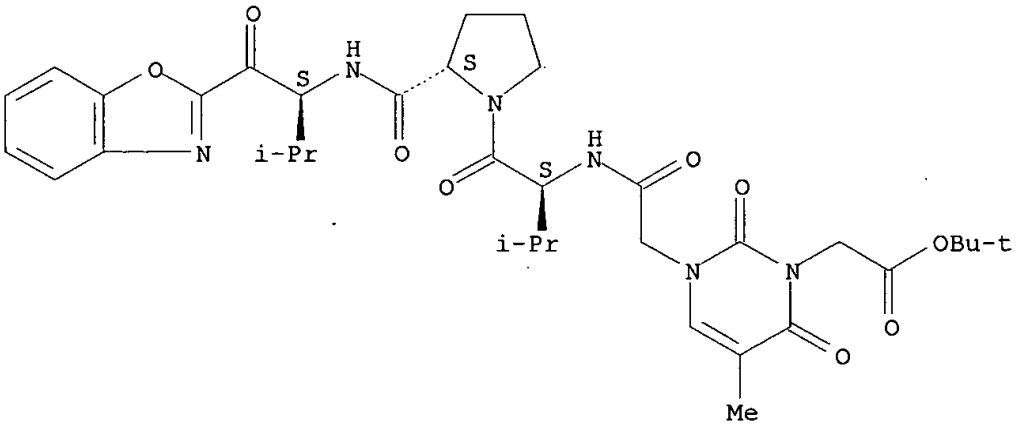
RN 291778-96-6 CAPLUS
CN L-Prolinamide, N-[[3-[2-(1,1-dimethylethoxy)-2-oxoethyl]-3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl]acetyl]-L-valyl-N-[(1S)-3-methoxy-1-(1-methylethyl)-2,3-dioxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 291779-04-9 CAPLUS
CN L-Prolinamide, N-[[3-[2-(1,1-dimethylethoxy)-2-oxoethyl]-3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl]acetyl]-L-valyl-N-[(1S)-1-(2-benzoxazolylcarbonyl)-2-methylpropyl]- (9CI) (CA INDEX NAME)

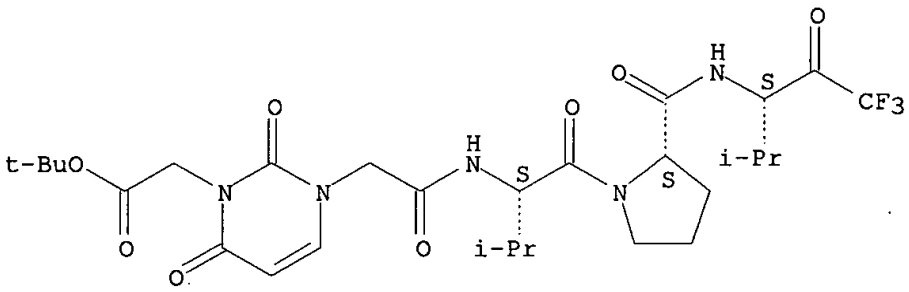
Absolute stereochemistry.



RN 291779-20-9 CAPLUS
CN L-Prolinamide, N-[[3-[2-(1,1-dimethylethoxy)-2-oxoethyl]-3,4-dihydro-2,4-

dioxo-1(2H)-pyrimidinyl]acetyl]-L-valyl-N-[(1S)-3,3,3-trifluoro-1-(1-methylethyl)-2-oxopropyl]- (9CI) (CA INDEX NAME)

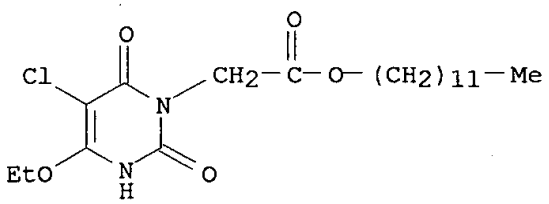
Absolute stereochemistry.



L8 ANSWER 7 OF 212 CAPLUS COPYRIGHT 2003 ACS
AN 2002:286044 CAPLUS
DN 136:316970
TI Heat-sensitive diazo recording material
IN Matsushita, Tetsunori; Yanagihara, Naoto; Takeuchi, Yosuke; Tsurumi, Mitsuyuki
PA Fuji Photo Film Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 55 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2002113953	A2	20020416	JP 2000-309578	20001010
PRAI JP 2000-309578		20001010		

OS MARPAT 136:316970
AB The material has a recording layer on a support, contg. a diazo compd. I [R1, R2 = H, (un)substituted alkyl or aryl; R3 = H, halo, substituted amino, (un)substituted alkyl, aryl, alkoxy, aryloxy, alkylthio, or arylthio; X- = acid anion] and a coupler II, III, or IV [X1 = O, S, imino; Y1-3, Z1, Z2 = C, O, N, S; X2 = OH, mercapto, or each (un)substituted alkoxy, aryloxy, alkylthio, arylthio, or amino; X3 = OH, mercapto, halo, CN, or each (un)substituted alkyl, aryl, alkoxy, aryloxy, alkylthio, arylthio, amino, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aryloxycarbonyl, alkylaminocarbonyl, arylaminocarbonyl, alkylaminosulfonyl, arylaminosulfonyl, alkylsulfonyl, arylsulfonyl, acyl, acylamino, alkylsulfonylamino, or arylsulfonylamino; Z3 = C, N; L1-3 = group releasable on coupling with the diazo compd.]. It showed high coupling speed and stability and improved color development.
IT **410097-04-0**
RL: TEM (Technical or engineered material use); USES (Uses)
(heat-sensitive diazo recording material contg. aminobenzenediazonium salt and coupler)
RN 410097-04-0 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 5-chloro-4-ethoxy-3,6-dihydro-2,6-dioxo-, dodecyl ester (9CI) (CA INDEX NAME)

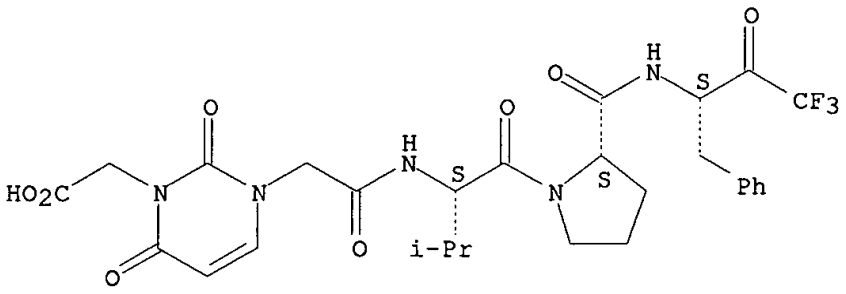


L8 ANSWER 8 OF 212 CAPLUS COPYRIGHT 2003 ACS
AN 2002:171894 CAPLUS
DN 136:217051
TI Preparation of proline derivatives for use as chymase inhibitor
IN Deguchi, Takashi; Shiratake, Ryotaro; Sato, Fuminori; Fujitani, Buichi; Honda, Yayoi; Kiyoshi, Akihiko; Notake, Mitsue; Showell, Graham Andrew; Boyle, Robert George; Klair, Sukhbinder Singh
PA Dainippon Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002018378	A1	20020307	WO 2001-JP7137	20010821
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2001078782	A5	20020313	AU 2001-78782	20010821
PRAI	GB 2000-21315	A	20000830		
	WO 2001-JP7137	W	20010821		

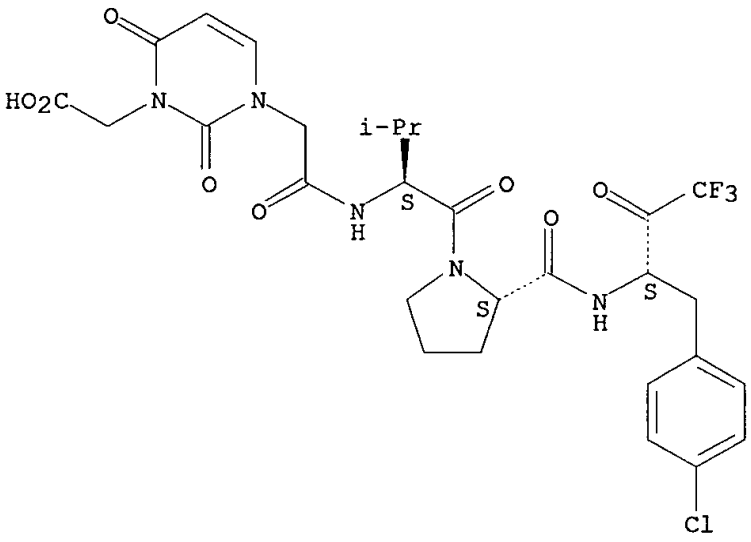
OS MARPAT 136:217051
AB Novel pyrrolidine derivs. I [R1 = cycloalkyl, Ph, naphthyl, tetrahydronaphthyl, indanyl, thienyl, furyl, indolyl, dihydroindolyl, benzofuryl, dihydrobenzofuryl, benzothienyl or an S-mono- or dioxide, or dihydrobenzothienyl, where the Ph, naphthyl and benzothienyl groups may have 1-3 substituents and the indolyl and dihydroindolyl groups may be N-substituted; R2 = H, alkyl, phenylalkyl, cycloalkyl, or cycloalkylalkyl; R3 is an (un)substituted monocyclic heterocyclic group, benzene- or pyridine-fused heterocyclic group, etc.; R4, R5 = H or OH, but both are not simultaneously H or both form oxo; n is 0-3] or their salts were prepd. as chymase inhibitors. Thus, N-[(1S)-2-[(2S)-2-[N-[(1S)-1-(benzo[b]thiophen-3-ylmethyl)-3,3,3-trifluoro-2-oxopropyl]carbamoyl]pyrrolidinyl]-1-(methylethyl)-2-oxoethyl](3,5-dimethylisoxazol-4-yl)carboxamide was prepd. via coupling reactions of (2S,3S)-3-amino-4-[benzo[b]thiophen-3-yl]-1,1,1-trifluoro-2-butanol hydrochloride, N-(tert-butoxycarbonyl)-L-valyl-L-proline, and 3,5-dimethyl-4-isoxazolecarboxylic acid and showed IC50 = 3.8 and 55 nM for inhibition of monkey or human chymase (in vitro assay).
IT **402733-13-5P 402733-14-6P 402733-15-7P 402733-16-8P 402733-17-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of proline derivs. for use as chymase inhibitors)
RN 402733-13-5 CAPLUS
CN L-Prolinamide, N-[[3-(carboxymethyl)-3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl]acetyl]-L-valyl-N-[(1S)-3,3,3-trifluoro-2-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



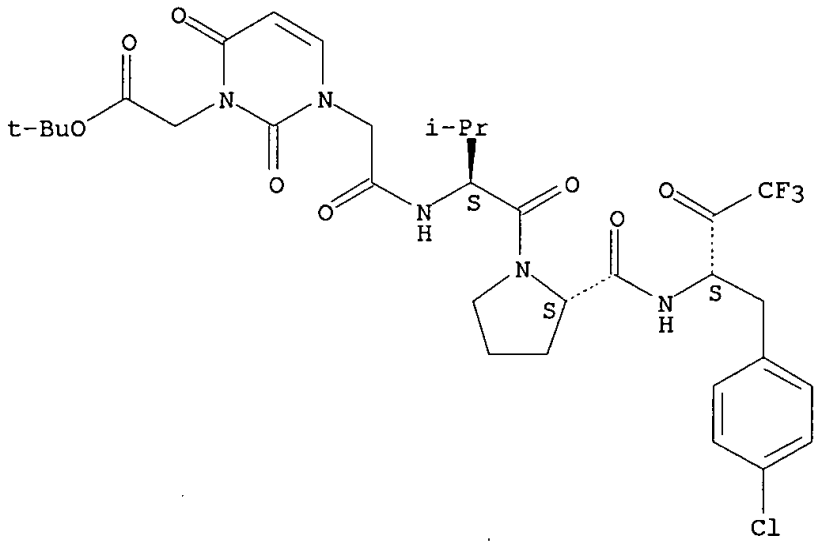
RN 402733-14-6 CAPLUS
CN L-Prolinamide, N-[[3-(carboxymethyl)-3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl]acetyl]-L-valyl-N-[(1S)-1-[(4-chlorophenyl)methyl]-3,3,3-trifluoro-2-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



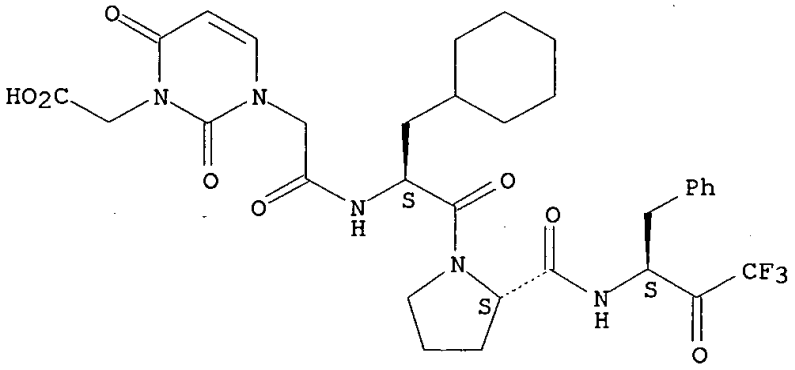
RN 402733-15-7 CAPLUS
CN L-Prolinamide, N-[[3-[2-(1,1-dimethylethoxy)-2-oxoethyl]-3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl]acetyl]-L-valyl-N-[(1S)-1-[(4-chlorophenyl)methyl]-3,3,3-trifluoro-2-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



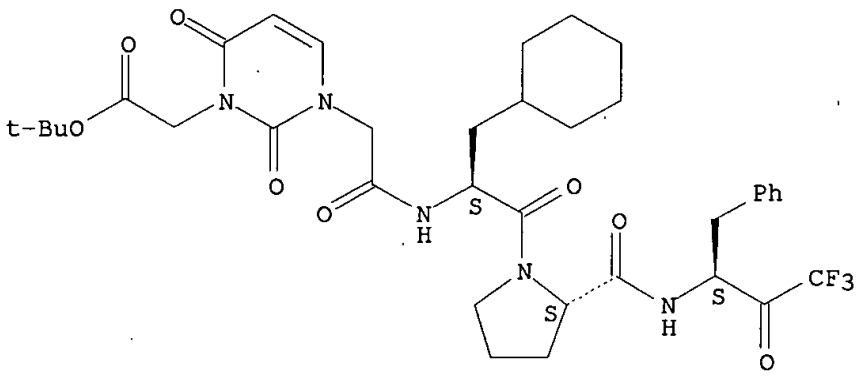
RN 402733-16-8 CAPLUS
CN L-Prolinamide, N-[[3-(carboxymethyl)-3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl]acetyl]-3-cyclohexyl-L-alanyl-N-[(1S)-3,3,3-trifluoro-2-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



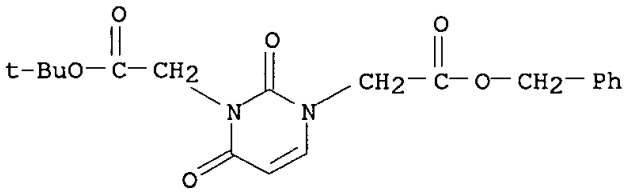
RN 402733-17-9 CAPLUS
CN L-Prolinamide, 3-cyclohexyl-N-[[3-[2-(1,1-dimethylethoxy)-2-oxoethyl]-3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl]acetyl]-L-alanyl-N-[(1S)-3,3,3-trifluoro-2-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

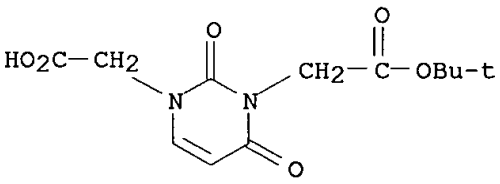


IT **291778-28-4P 291778-30-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of proline derivs. for use as chymase inhibitors)

RN 291778-28-4 CAPLUS
CN 1,3(2H,4H)-Pyrimidinediacetic acid, 2,4-dioxo-, .alpha.3-(1,1-dimethylethyl) .alpha.1-(phenylmethyl) ester (9CI) (CA INDEX NAME)



RN 291778-30-8 CAPLUS
CN 1,3(2H,4H)-Pyrimidinediacetic acid, 2,4-dioxo-, .alpha.3-(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 212 CAPLUS COPYRIGHT 2003 ACS
AN 2002:84598 CAPLUS
DN 136:102658
TI Preparation of aromatic heterocyclic derivatives as enzyme inhibitors
IN Brunck, Terence Kevin; Tamura, Susan Y.; Semple, Joseph Edward; Ardecky, Robert John; Ge, Yu; Ripka, William Charles
PA Corvas International, Inc., USA
SO U.S., 84 pp., Cont.-in-part of U.S. 6,011,158.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6342504	B1	20020129	US 1999-194855	19991221
	US 5656645	A	19970812	US 1995-484506	19950607
	US 5658930	A	19970819	US 1995-481660	19950607
	WO 9618644	A1	19960620	WO 1995-US16410	19951213
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	US 6008351	A	19991228	US 1995-573775	19951218
	US 6011158	A	20000104	US 1996-659983	19960607
	WO 9746207	A2	19971211	WO 1997-US9818	19970609
	WO 9746207	A3	19980423		
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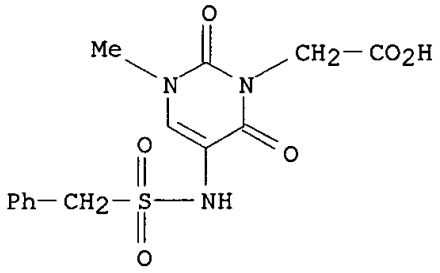
PRAI	US 1994-356833	A2	19941213		
	US 1995-481660	A2	19950607		
	US 1995-484506	A2	19950607		
	WO 1995-US16410	A2	19951213		
	US 1995-573775	A2	19951218		
	US 1996-659983	A2	19960607		
	WO 1997-US9818	W	19970609		

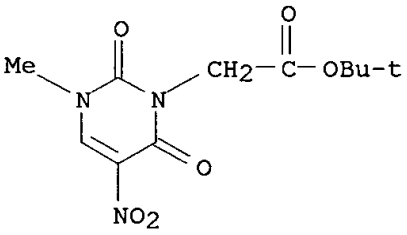
OS MARPAT 136:102658
AB Peptide aldehydes R1-X-NH-Het-CHR2CONHCH(CH2R3)CHO-(S) [X = SO2, NR'SO2 (R' = H, alkyl, aryl, aralkyl), CO, O2C, NHCO, P(O)R'' (R'' = NR', OR', R', SR') or a direct link; R1 = (un)substituted alkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, etc.; R2 = H, alkyl, alkenyl; R3 = 2-guanidinoethyl, 3-amidinocyclohexyl or -Ph, or 1-amidino-3-piperidinyl; Het = substituted 2-oxo-1,3-pyridinediyl, 6-oxo-1,5-pyrimidinediyl or 2,4-dioxo-1,5-pyrimidinediyl] were prepd. as thrombin inhibitors. Thus, N-[3-[(benzylsulfonyl)amino]-2-oxo-1,2-dihydropyridyl]acetyl-L-argininal, prepd. by a multistep procedure which starts with conversion of N.alpha.-tert-butoxycarbonyl-N.gamma.-nitroarginine to the lactam, showed Ki = 289 .+-. 32 pM for inhibition of human .alpha.-thrombin amidolytic activity.
IT **179524-01-7P 179524-45-9P 179524-46-0P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of arom. heterocyclic derivs. as enzyme inhibitors)

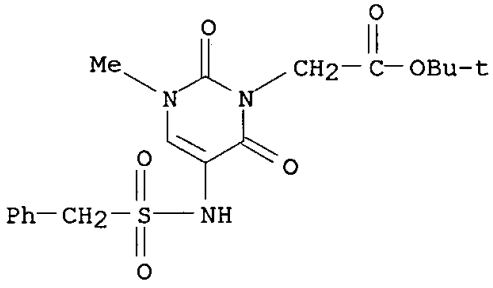
RN 179524-01-7 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 3,6-dihydro-3-methyl-2,6-dioxo-5-[[(phenylmethyl)sulfonyl]amino]- (9CI) (CA INDEX NAME)



RN 179524-45-9 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 3,6-dihydro-3-methyl-5-nitro-2,6-dioxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



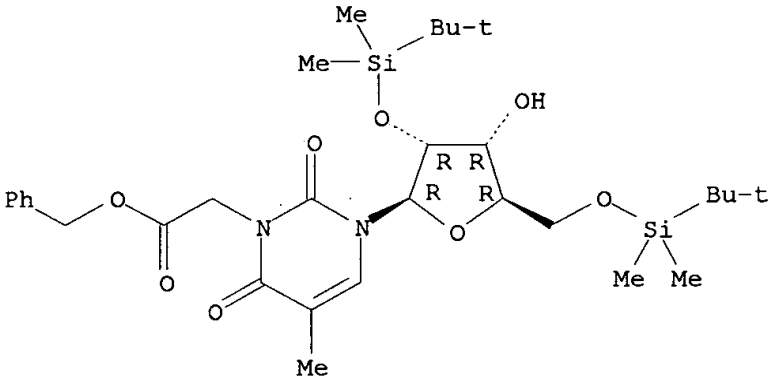
RN 179524-46-0 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 3,6-dihydro-3-methyl-2,6-dioxo-5-[[(phenylmethyl)sulfonyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

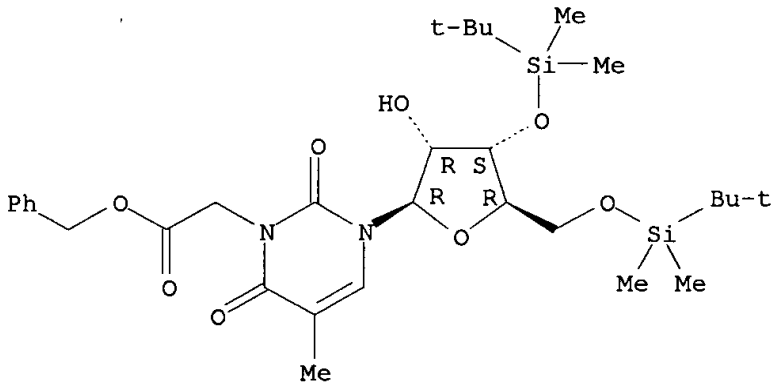
L8 ANSWER 10 OF 212 CAPLUS COPYRIGHT 2003 ACS
AN 2001:872209 CAPLUS
DN 136:200401
TI Identification of a novel family of nucleosides that specifically inhibit HIV-1 reverse transcriptase
AU Chamorro, Cristina; Lobaton, Esther; Bonache, Maria-Cruz; De Clercq, Erik; Balzarini, Jan; Velazquez, Sonsoles; San-Felix, Ana; Camarasa, Maria-Jose
CS Instituto de Quimica Medica (C.S.I.C.), Madrid, 28006, Spain
SO Bioorganic & Medicinal Chemistry Letters (2001), 11(23), 3085-3088
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
AB N-3-Benzyloxycarbonylmethyl- and N-3-carboxymethyl-TBDMS-substituted nucleosides were synthesized and evaluated for activity against HIV replication. It was found that the N-3-carboxymethyl-TBDMS-substituted nucleosides were specific inhibitors of HIV-1 replication. They should be considered as members of a novel and original class of NNRTIs.
IT **401515-18-2P 401515-19-3P 401515-20-6P**
401515-21-7P 401515-26-2P 401515-28-4P
401515-30-8P 401515-32-0P 401515-33-1P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of a novel family of N-3-carboxymethyl-TBDMS-substituted nucleosides that specifically inhibit HIV reverse transcriptase)
RN 401515-18-2 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 3-[2,5-bis-O-[(1,1-dimethylethyl)dimethylsilyl]-.beta.-D-ribofuranosyl]-3,6-dihydro-5-methyl-2,6-dioxo-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



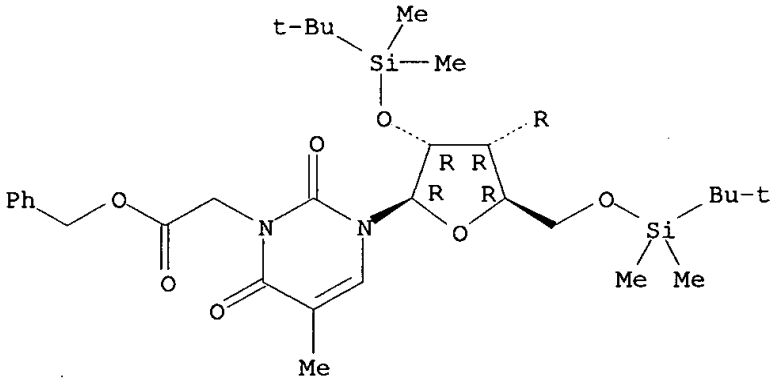
RN 401515-19-3 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 3-[3,5-bis-O-[(1,1-dimethylethyl)dimethylsilyl]-.beta.-D-ribofuranosyl]-3,6-dihydro-5-methyl-2,6-dioxo-, phenylmethyl ester (9CI) (CA INDEX NAME)

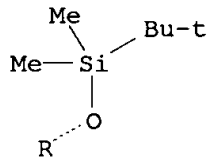
Absolute stereochemistry.



RN 401515-20-6 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 3,6-dihydro-5-methyl-2,6-dioxo-3-[2,3,5-tris-O-[(1,1-dimethylethyl)dimethylsilyl]-.beta.-D-ribofuranosyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

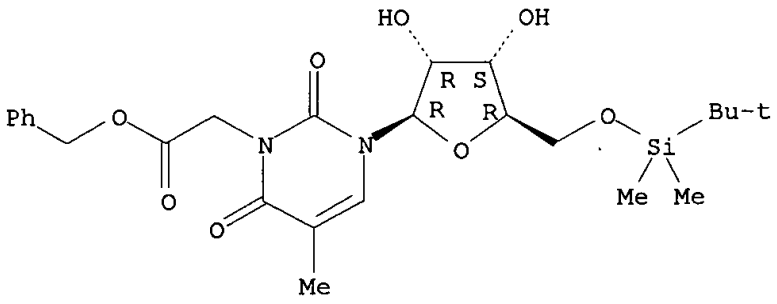
Absolute stereochemistry.





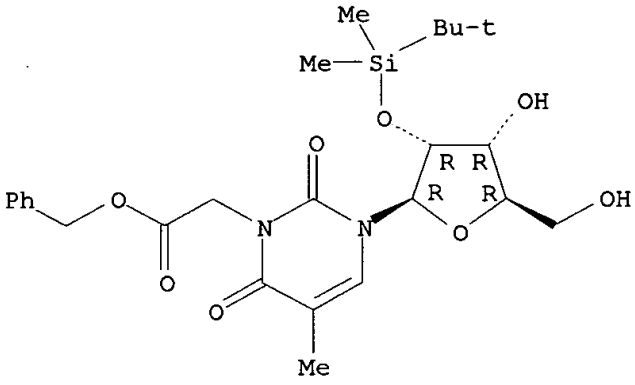
RN 401515-21-7 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 3-[5-O-[(1,1-dimethylethyl)dimethylsilyl]-.beta.-D-ribofuranosyl]-3,6-dihydro-5-methyl-2,6-dioxo-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



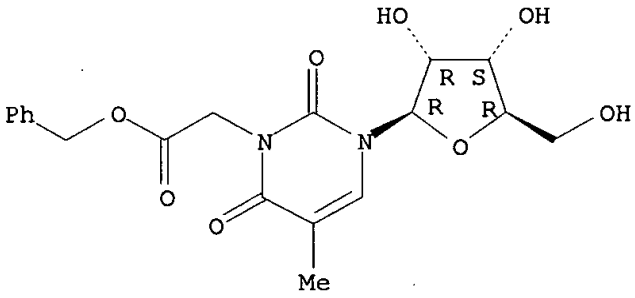
RN 401515-26-2 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 3-[2-O-[(1,1-dimethylethyl)dimethylsilyl]-.beta.-D-ribofuranosyl]-3,6-dihydro-5-methyl-2,6-dioxo-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



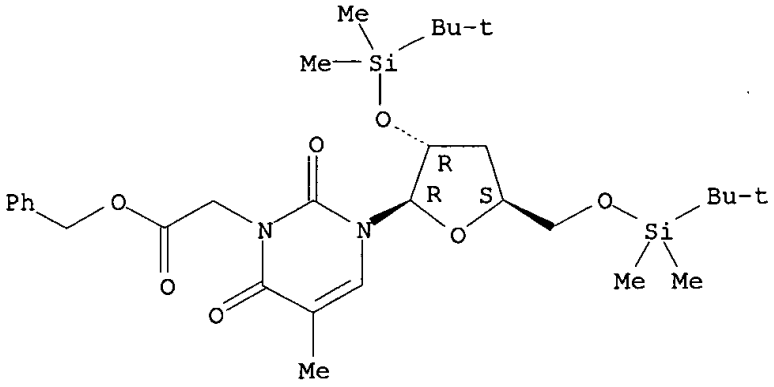
RN 401515-28-4 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 3,6-dihydro-5-methyl-2,6-dioxo-3-.beta.-D-ribofuranosyl-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



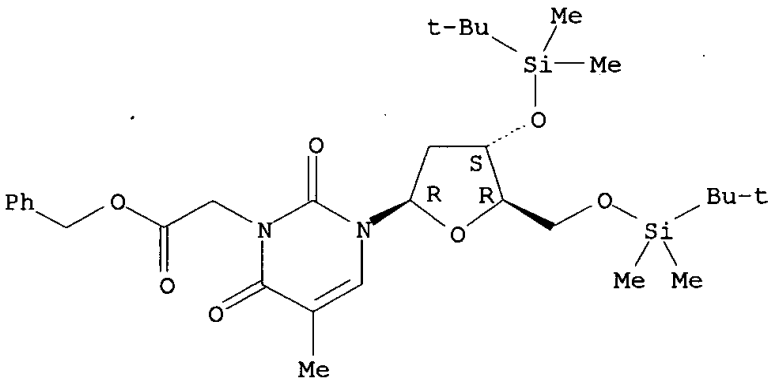
RN 401515-30-8 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 3-[3-deoxy-2,5-bis-O-[(1,1-dimethylethyl)dimethylsilyl]-.beta.-D-erythro-pentofuranosyl]-3,6-dihydro-5-methyl-2,6-dioxo-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



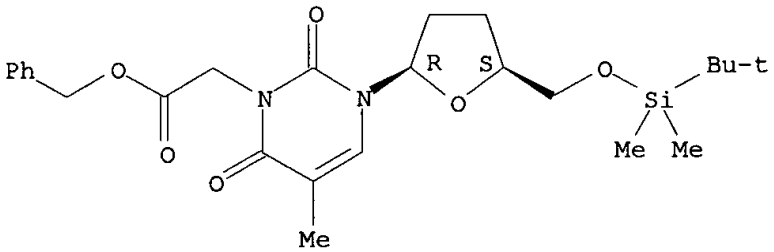
RN 401515-32-0 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 3-[2-deoxy-3,5-bis-O-[(1,1-dimethylethyl)dimethylsilyl]-.beta.-D-erythro-pentofuranosyl]-3,6-dihydro-5-methyl-2,6-dioxo-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 401515-33-1 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 3-[(2R,5S)-5-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]tetrahydro-2-furanyl]-3,6-dihydro-5-methyl-2,6-dioxo-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

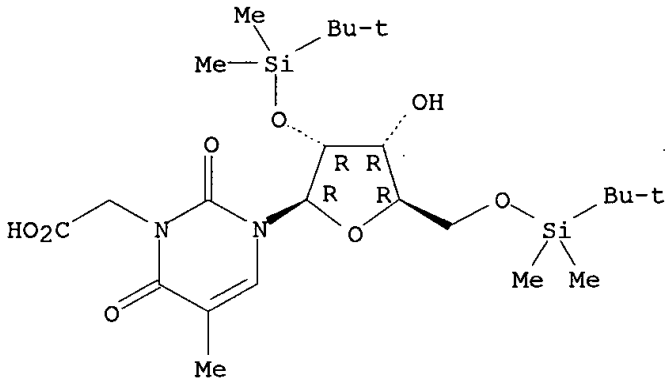


IT **401515-22-8P 401515-23-9P 401515-24-0P**

401515-25-1P 401515-27-3P 401515-29-5P
401515-31-9P 401515-34-2P 401515-35-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of a novel family of N-3-carboxymethyl-TBDMS-substituted nucleosides that specifically inhibit HIV reverse transcriptase)

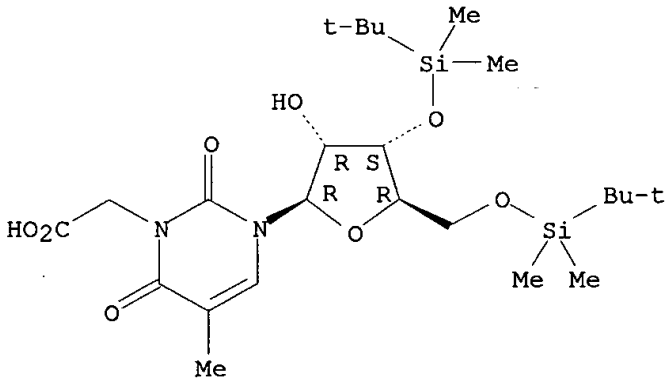
RN 401515-22-8 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 3-[2,5-bis-O-[(1,1-dimethylethyl)dimethylsilyl]-.beta.-D-ribofuranosyl]-3,6-dihydro-5-methyl-2,6-dioxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



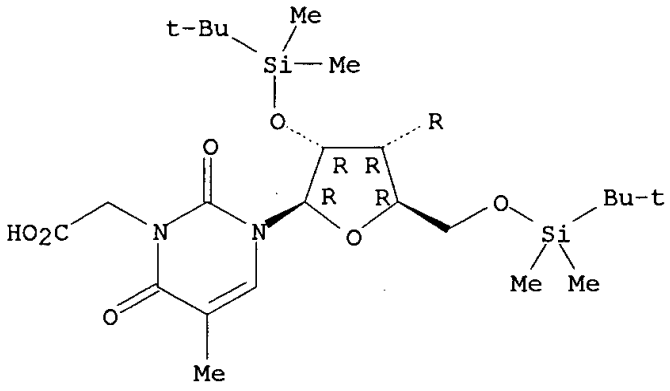
RN 401515-23-9 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 3-[3,5-bis-O-[(1,1-dimethylethyl)dimethylsilyl]-.beta.-D-ribofuranosyl]-3,6-dihydro-5-methyl-2,6-dioxo- (9CI) (CA INDEX NAME)

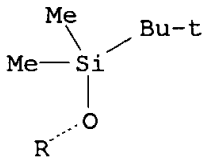
Absolute stereochemistry.



RN 401515-24-0 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 3,6-dihydro-5-methyl-2,6-dioxo-3-[2,3,5-tris-O-[(1,1-dimethylethyl)dimethylsilyl]-.beta.-D-ribofuranosyl]- (9CI) (CA INDEX NAME)

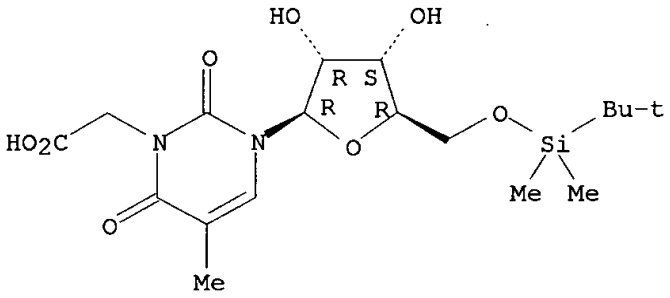
Absolute stereochemistry.





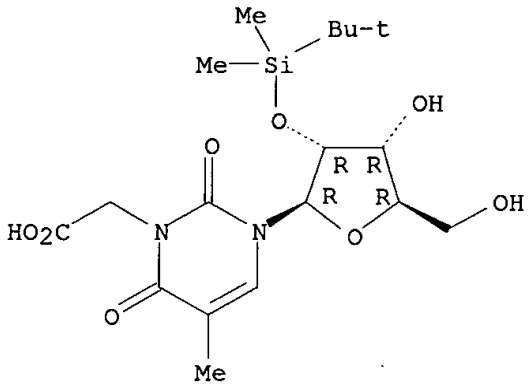
RN 401515-25-1 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 3-[5-O-[(1,1-dimethylethyl)dimethylsilyl]-.beta.-D-ribofuranosyl]-3,6-dihydro-5-methyl-2,6-dioxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



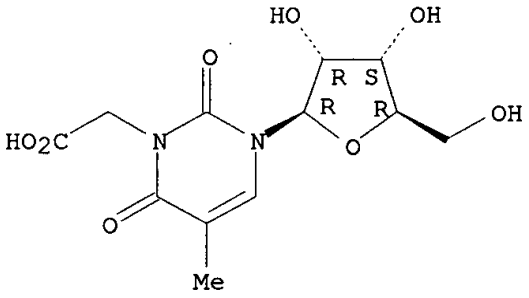
RN 401515-27-3 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 3-[2-O-[(1,1-dimethylethyl)dimethylsilyl]-.beta.-D-ribofuranosyl]-3,6-dihydro-5-methyl-2,6-dioxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



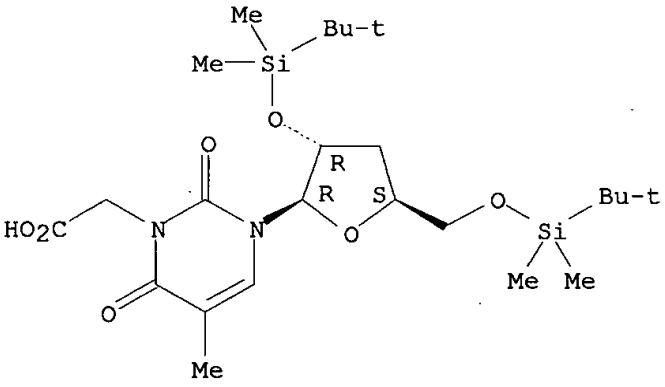
RN 401515-29-5 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 3,6-dihydro-5-methyl-2,6-dioxo-3-.beta.-D-ribofuranosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 401515-31-9 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 3-[3-deoxy-2,5-bis-O-[(1,1-dimethylethyl)dimethylsilyl]-.beta.-D-erythro-pentofuranosyl]-3,6-dihydro-5-methyl-2,6-dioxo- (9CI) (CA INDEX NAME)

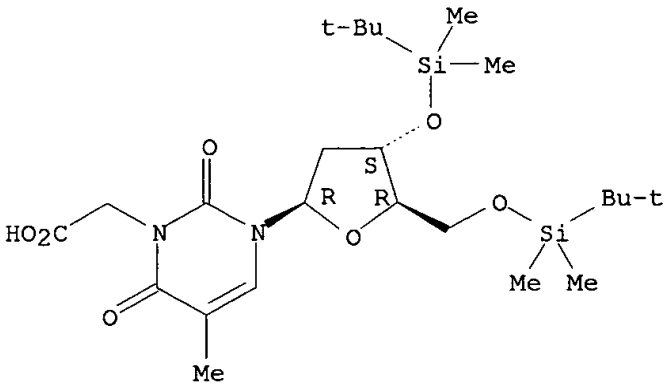
Absolute stereochemistry.



RN 401515-34-2 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 3-[2-deoxy-3,5-bis-O-[(1,1-

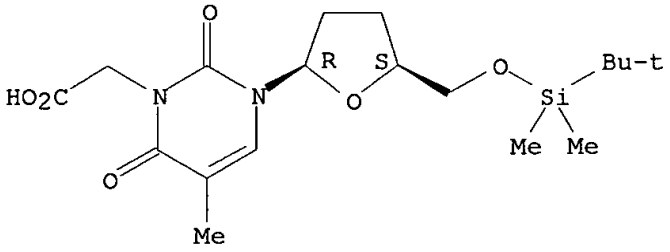
dimethylethyl)dimethylsilyl]-.beta.-D-erythro-pentofuranosyl]-3,6-dihydro-5-methyl-2,6-dioxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 401515-35-3 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 3-[(2R,5S)-5-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]tetrahydro-2-furanyl]-3,6-dihydro-5-methyl-2,6-dioxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> s l7/thu
           212 L7
        503172 THU/RL
L21          19 L7/THU
                (L7 (L) THU/RL)

=> d l21 1-19 bib,ab,hitstr
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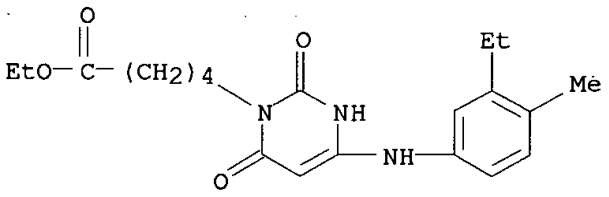
L21 ANSWER 1 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 2003:117630 CAPLUS
DN 138:170246
TI Preparation of N3-substituted 6-anilinopyrimidines to treat Gram-positive bacterial and mycoplasmal infections
IN Zhi, Chengxin; Long, Zheng-Yu; Wright, George E.; Brown, Neal C.
PA University of Massachusetts, USA; Shire Biochem Inc.
SO PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003011297	A1	20030213	WO 2002-US19398	20020617

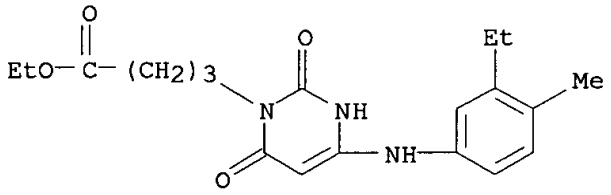
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-298357P P 20010615
US 2002-348420P P 20020114
OS MARPAT 138:170246
AB The title compds. [I; R1 = (CH2)m[An(CH2)p]qB (wherein A = CH2, CH:CH, CO, etc.; B = H, halo, alkyl, etc.; m = 1-4; n = 0-1; p = 0-4; q = 0-4); R2, R3 = alkyl, alkenyl, halo; or R2 and R3 together are alkylene; with the provisos], useful for treating Gram-pos. bacterial and mycoplasmal infections, were prepd. Thus, reacting 6-amino-2-methoxy-3-[2-(2-benzyloxyethoxy)ethyl]-4-pyrimidone with 3-ethyl-4-methylaniline.HCl afforded 72% I [R1 = (CH2)2O(CH2)2OCH2Ph; R2 = Et; R3 = Me] which showed MIC of 5 .mu.g/mL against S. aureus and E. fecalis.
IT **478921-24-3P**, 3-(4-(Ethoxycarbonyl)butyl)-6-(3-ethyl-4-methylanilino)uracil **480446-12-6P 496942-89-3P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of N3-substituted 6-anilinopyrimidines to treat Gram-pos. bacterial and mycoplasmal infections)
RN 478921-24-3 CAPLUS
CN 1(2H)-Pyrimidinepentanoic acid, 4-[(3-ethyl-4-methylphenyl)amino]-3,6-dihydro-2,6-dioxo-, ethyl ester (9CI) (CA INDEX NAME)

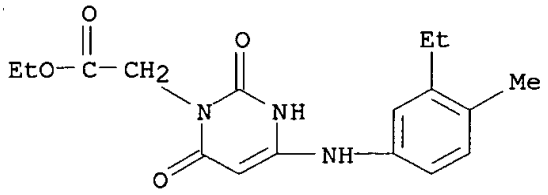


RN 480446-12-6 CAPLUS
CN 1(2H)-Pyrimidinebutanoic acid, 4-[(3-ethyl-4-methylphenyl)amino]-3,6-

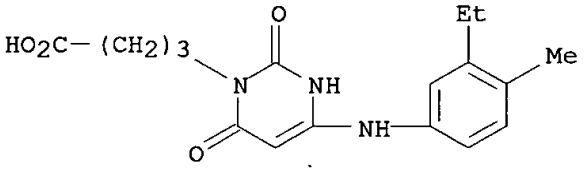
dihydro-2,6-dioxo-, ethyl ester (9CI) (CA INDEX NAME)



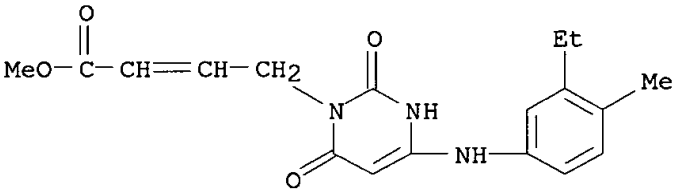
RN 496942-89-3 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 4-[(3-ethyl-4-methylphenyl)amino]-3,6-dihydro-2,6-dioxo-, ethyl ester (9CI) (CA INDEX NAME)



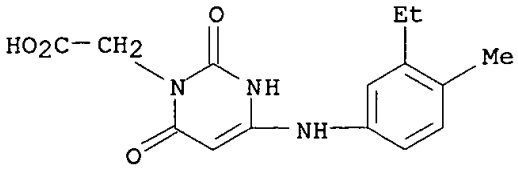
IT **480446-16-0P 496942-85-9P 496942-99-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N3-substituted 6-anilinopyrimidines to treat Gram-pos. bacterial and mycoplasmal infections)
RN 480446-16-0 CAPLUS
CN 1(2H)-Pyrimidinebutanoic acid, 4-[(3-ethyl-4-methylphenyl)amino]-3,6-dihydro-2,6-dioxo- (9CI) (CA INDEX NAME)



RN 496942-85-9 CAPLUS
CN 2-Butenoic acid, 4-[4-[(3-ethyl-4-methylphenyl)amino]-3,6-dihydro-2,6-dioxo-1(2H)-pyrimidinyl]-, methyl ester (9CI) (CA INDEX NAME)

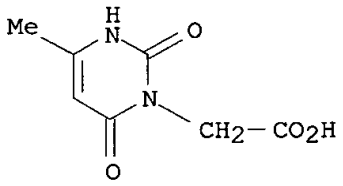


RN 496942-99-5 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 4-[(3-ethyl-4-methylphenyl)amino]-3,6-dihydro-2,6-dioxo- (9CI) (CA INDEX NAME)



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 2002:725916 CAPLUS
TI (6-Methyl-2-methylsulfanyl-4-oxo-3,4-dihydro-3-pyrimidinyl)acetic acid and related compounds exhibiting anti-inflammatory activity
AU Jakubkiene, V.; Burbuliene, M. M.; Udrenaite, E.; Garaliene, V.; Vainilavicius, P.
CS Fac. of Chemistry, Vilnius Univ., Lithuania
SO Pharmazie (2002), 57(9), 610-613
CODEN: PHARAT; ISSN: 0031-7144
PB Govi-Verlag Pharmazeutischer Verlag GmbH
DT Journal
LA English
AB Base-promoted hydrolysis of Me or Et esters 1a-c gave the (6-methyl-2-methylsulfanyl-4-oxo-3,4-dihydro-3-pyrimidinyl)- and (5-ethyl-6-methyl-2-methylsulfanyl-4-oxo-3,4-dihydro-3-pyrimidinyl)acetic acids 2a, b. Under the reaction of ester 1a or acid 2a with nucleophilic reagents a series of derivs. 3-7 of acid 2a were synthesized and evaluated for their anti-inflammatory activity. Most of them were found to be more active than acetylsalicylic acid, and compds. 2a, 6a, b, 7a, f were significantly more active than ibuprofen. The compds. exhibiting the best anti-inflammatory activity showed neg. inotropic effect.
IT **54069-85-1**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(prepn. of (6-Me-2-methylsulfanyl-4-oxo-3,4-dihydro-3-pyrimidinyl)acetic acid and related compds. and their anti-inflammatory and neg. inotropic activity)
RN 54069-85-1 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 3,6-dihydro-4-methyl-2,6-dioxo- (9CI) (CA INDEX NAME)



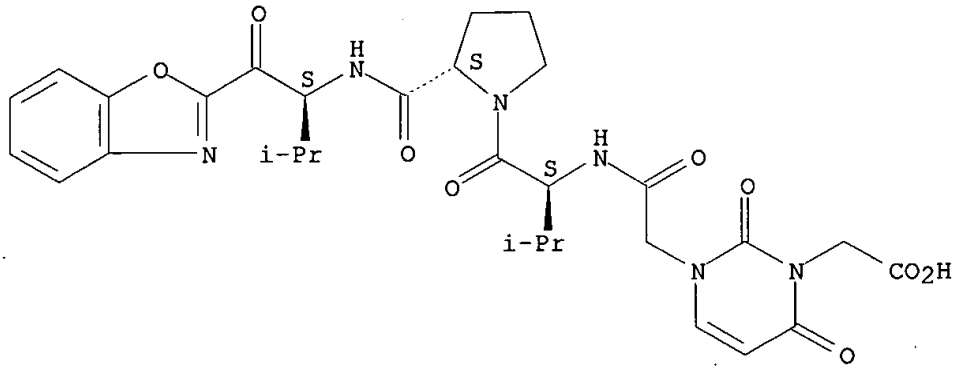
RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 2002:359856 CAPLUS
DN 136:369997
TI Pharmaceuticals containing heterocyclyl group-containing prolines as water-soluble inhibitors of human neutrophil elastase
IN Sato, Fuminori; Inoue, Yasuharu; Omotani, Tomoki; Shiratake, Ryotaro; Honda, Seiji; Komiya, Masanobu; Takemura, Tadashi
PA Dainippon Pharmaceutical Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 41 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2002138048	A2	20020514	JP 2001-251265	20010822
PRAI JP 2000-254746	A	20000825		

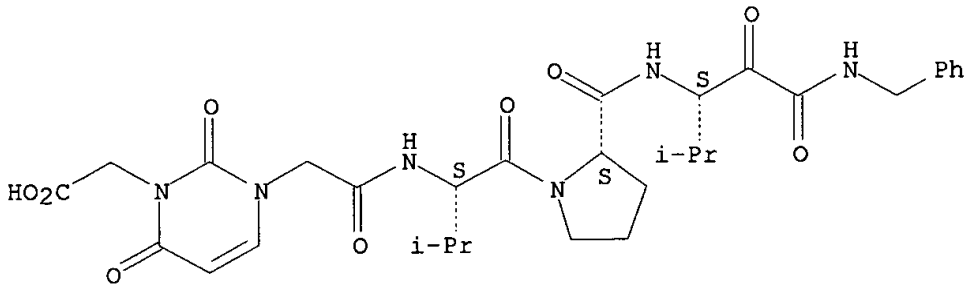
OS MARPAT 136:369997
AB Title compds. I [A, B = (oxo-substituted) lower alkylene D = Q; D1 = (oxo-substituted) CH2, (oxo-substituted) CH2CH2; the ring G = 5- to 14-membered monocyclic (un)satd. (un)substituted heterocycle reside (having addnl. N, O, and/or S); R1, R2 = lower alkyl; R3 = (CX1X2)n(CH2)mY1; X1, X2 = halo; Y1 = H, halo, lower alkoxycarbonyl, lower alkylaminocarbonyl, etc.] or their physiol. acceptable salts are prepd. and are esp. useful for therapeutic and prophylactic treatment of acute lung disease, e.g. emphysema and acute respiratory distress syndrome. Thus, condensation of 2-[(3-tert-butoxycarbonylmethyl-2-oxo-1-imidazolidinyl)]acetic acid with L-valyl-N-[(1S,2S)-(3,3,3-trifluoro-1-isopropyl-2-hydroxypropyl)]-L-prolinamide HCl salt gave the corresponding amide, which was oxidized with Dess-Martin reagent and deprotected to afford 2-(3-carboxymethyl-2-oxo-1-imidazolidinyl)acetyl-L-valyl-N-[(1S)-3,3,3-trifluoro-1-isopropyl-2-oxopropyl]-L-prolinamide. The product inhibited human neutrophil elastase at IC50 value of 0.010 .mu.M and showed much better water soly. than ONO-5046.
IT **291778-79-5P 291778-80-8P**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of heterocyclyl group-contg. prolines as water-sol. inhibitors of human neutrophil elastase)
RN 291778-79-5 CAPLUS
CN L-Prolinamide, N-[[3-(carboxymethyl)-3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl]acetyl]-L-valyl-N-[(1S)-1-(2-benzoxazolylcarbonyl)-2-methylpropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



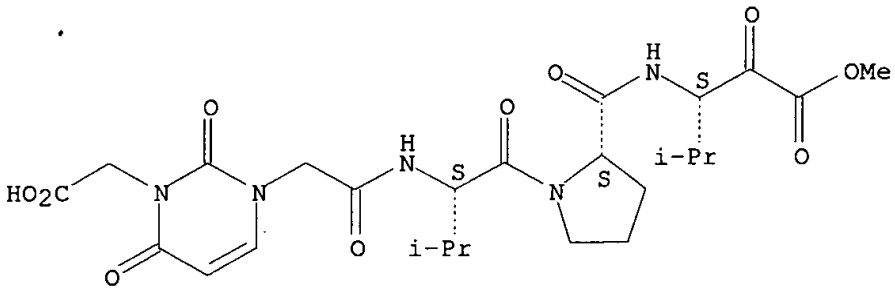
RN 291778-80-8 CAPLUS
CN L-Prolinamide, N-[[3-(carboxymethyl)-3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl]acetyl]-L-valyl-N-[(1S)-1-(1-methylethyl)-2,3-dioxo-3-[(phenylmethyl)amino]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



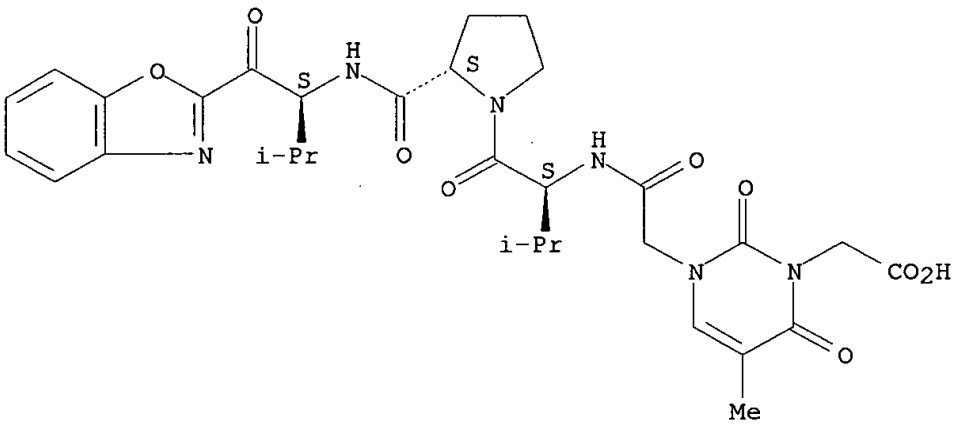
IT **291778-95-5P 291779-03-8P 291779-19-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of heterocyclyl group-contg. prolines as water-sol. inhibitors of human neutrophil elastase)
RN 291778-95-5 CAPLUS
CN L-Prolinamide, N-[[3-(carboxymethyl)-3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl]acetyl]-L-valyl-N-[(1S)-3-methoxy-1-(1-methylethyl)-2,3-dioxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



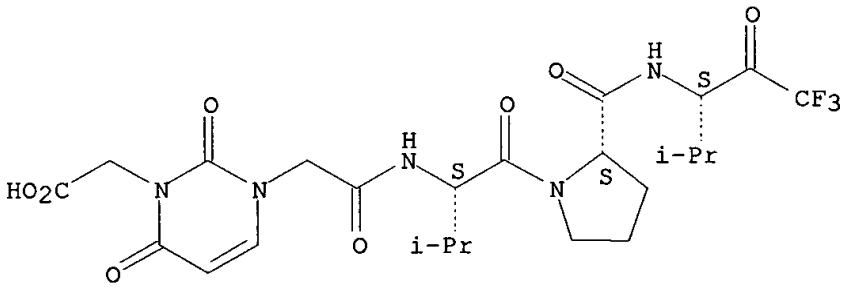
RN 291779-03-8 CAPLUS
CN L-Prolinamide, N-[[3-(carboxymethyl)-3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl]acetyl]-L-valyl-N-[(1S)-1-(2-benzoxazolylcarbonyl)-2-methylpropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 291779-19-6 CAPLUS
CN L-Prolinamide, N-[[3-(carboxymethyl)-3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl]acetyl]-L-valyl-N-[(1S)-3,3,3-trifluoro-1-(1-methylethyl)-2-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



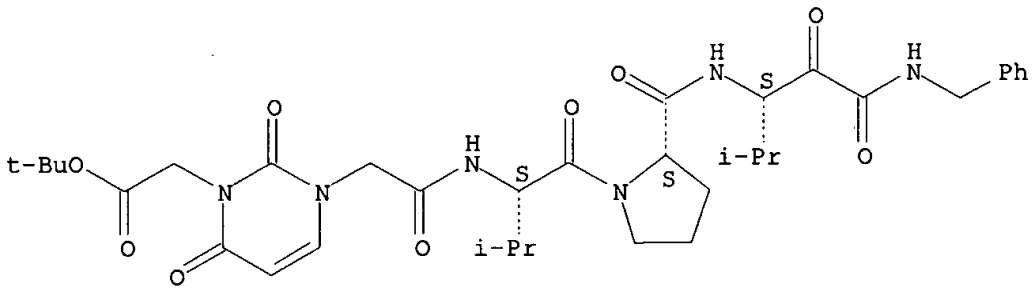
IT **291778-81-9P 291778-96-6P 291779-04-9P 291779-20-9P**

RL: SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of heterocyclyl group-contg. prolines as water-sol. inhibitors of human neutrophil elastase)

RN 291778-81-9 CAPLUS

CN L-Prolinamide, N-[[3-[2-(1,1-dimethylethoxy)-2-oxoethyl]-3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl]acetyl]-L-valyl-N-[(1S)-1-(1-methylethyl)-2,3-dioxo-3-[(phenylmethyl)amino]propyl]- (9CI) (CA INDEX NAME)

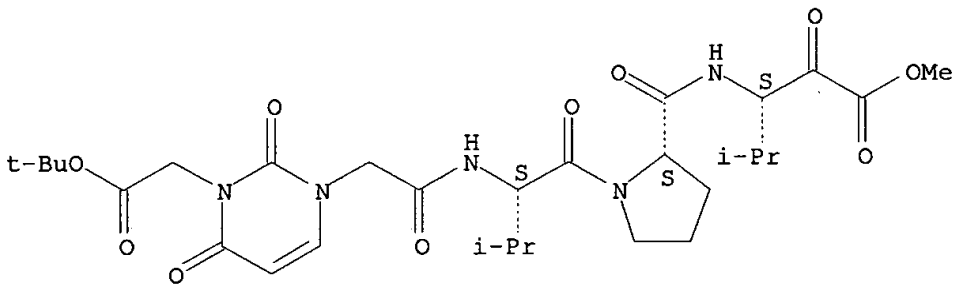
Absolute stereochemistry.



RN 291778-96-6 CAPLUS

CN L-Prolinamide, N-[[3-[2-(1,1-dimethylethoxy)-2-oxoethyl]-3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl]acetyl]-L-valyl-N-[(1S)-3-methoxy-1-(1-methylethyl)-2,3-dioxopropyl]- (9CI) (CA INDEX NAME)

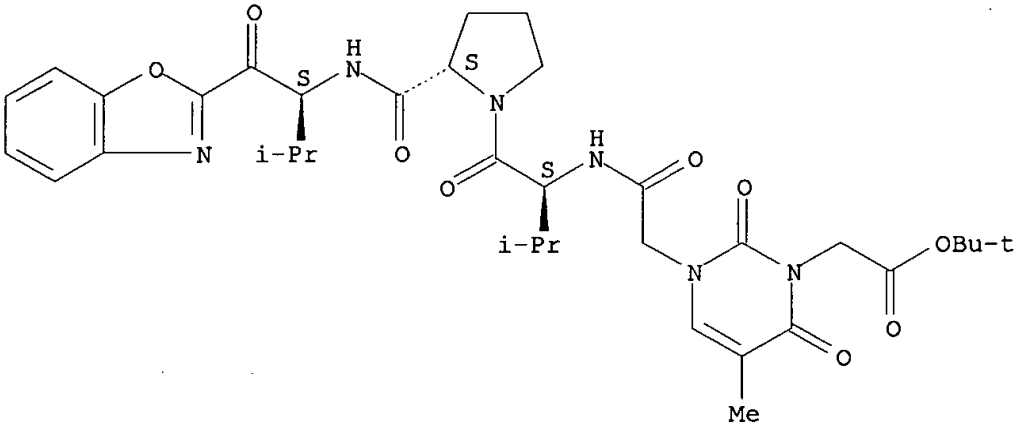
Absolute stereochemistry.



RN 291779-04-9 CAPLUS

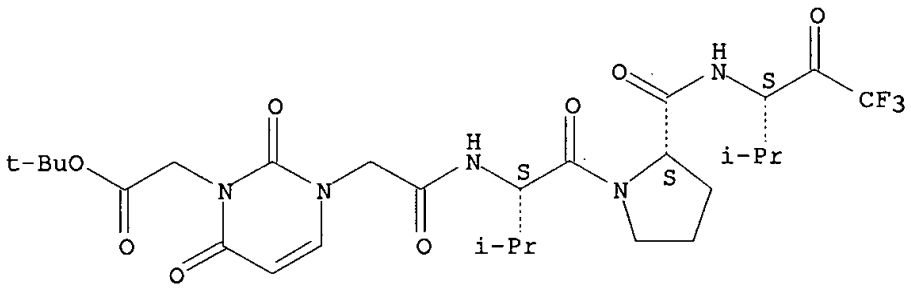
CN L-Prolinamide, N-[[3-[2-(1,1-dimethylethoxy)-2-oxoethyl]-3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl]acetyl]-L-valyl-N-[(1S)-1-(2-benzoxazolylcarbonyl)-2-methylpropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 291779-20-9 CAPLUS
CN L-Prolinamide, N-[[3-[2-(1,1-dimethylethoxy)-2-oxoethyl]-3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl]acetyl]-L-valyl-N-[(1S)-3,3,3-trifluoro-1-(1-methylethyl)-2-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

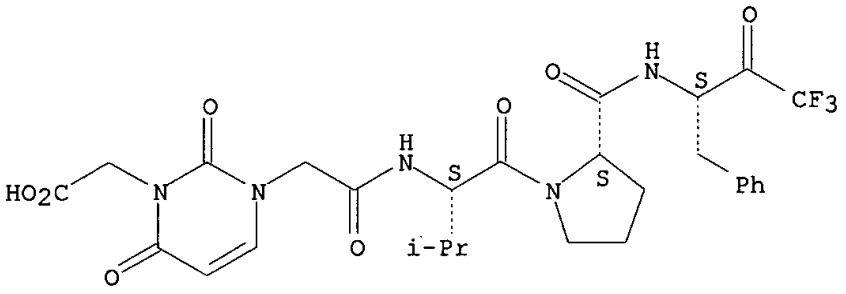


L21 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 2002:171894 CAPLUS
DN 136:217051
TI Preparation of proline derivatives for use as chymase inhibitor
IN Deguchi, Takashi; Shiratake, Ryotaro; Sato, Fuminori; Fujitani, Buichi; Honda, Yayoi; Kiyoshi, Akihiko; Notake, Mitsue; Showell, Graham Andrew; Boyle, Robert George; Klair, Sukhbinder Singh
PA Dainippon Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002018378	A1	20020307	WO 2001-JP7137	20010821
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2001078782	A5	20020313	AU 2001-78782	20010821
PRAI	GB 2000-21315	A	20000830		
	WO 2001-JP7137	W	20010821		

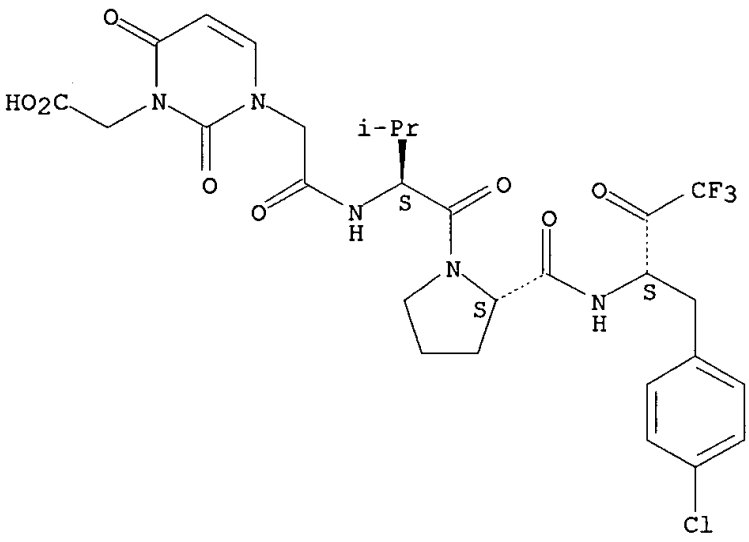
OS MARPAT 136:217051
AB Novel pyrrolidine derivs. I [R1 = cycloalkyl, Ph, naphthyl, tetrahydronaphthyl, indanyl, thienyl, furyl, indolyl, dihydroindolyl, benzofuryl, dihydrobenzofuryl, benzothienyl or an S-mono- or dioxide, or dihydrobenzothienyl, where the Ph, naphthyl and benzothienyl groups may have 1-3 substituents and the indolyl and dihydroindolyl groups may be N-substituted; R2 = H, alkyl, phenylalkyl, cycloalkyl, or cycloalkylalkyl; R3 is an (un)substituted monocyclic heterocyclic group, benzene- or pyridine-fused heterocyclic group, etc.; R4, R5 = H or OH, but both are not simultaneously H or both form oxo; n is 0-3] or their salts were prepd. as chymase inhibitors. Thus, N-[(1S)-2-[(2S)-2-[N-[(1S)-1-(benzo[b]thiophen-3-ylmethyl)-3,3,3-trifluoro-2-oxopropyl]carbamoyl]pyrrolidinyl]-1-(methylethyl)-2-oxoethyl](3,5-dimethylisoxazol-4-yl)carboxamide was prepd. via coupling reactions of (2S,3S)-3-amino-4-[benzo[b]thiophen-3-yl]-1,1,1-trifluoro-2-butanol hydrochloride, N-(tert-butoxycarbonyl)-L-valyl-L-proline, and 3,5-dimethyl-4-isoxazolecarboxylic acid and showed IC50 = 3.8 and 55 nM for inhibition of monkey or human chymase (in vitro assay).
IT **402733-13-5P 402733-14-6P 402733-15-7P 402733-16-8P 402733-17-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of proline derivs. for use as chymase inhibitors)
RN 402733-13-5 CAPLUS
CN L-Prolinamide, N-[[3-(carboxymethyl)-3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl]acetyl]-L-valyl-N-[(1S)-3,3,3-trifluoro-2-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



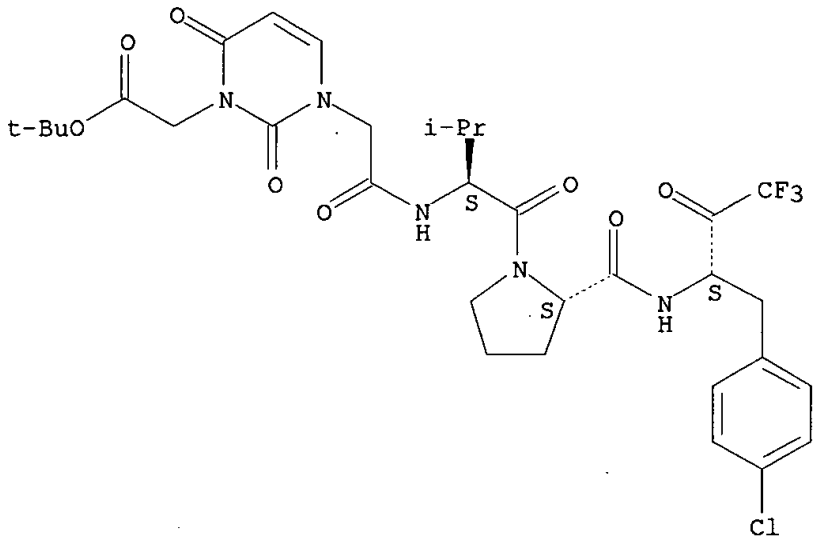
RN 402733-14-6 CAPLUS
CN L-Prolinamide, N-[[3-(carboxymethyl)-3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl]acetyl]-L-valyl-N-[(1S)-1-[(4-chlorophenyl)methyl]-3,3,3-trifluoro-2-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



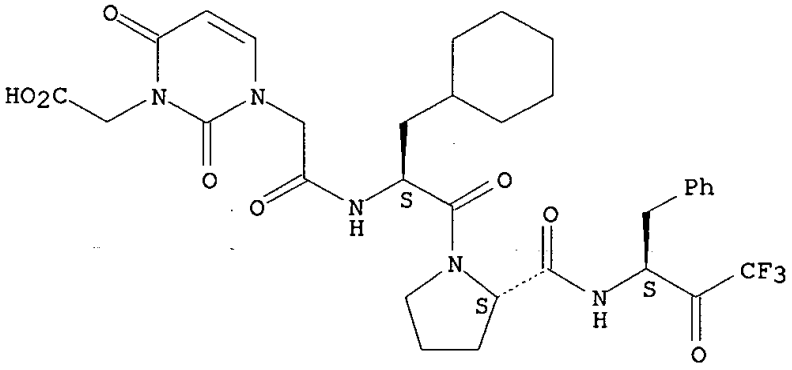
RN 402733-15-7 CAPLUS
CN L-Prolinamide, N-[[3-[2-(1,1-dimethylethoxy)-2-oxoethyl]-3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl]acetyl]-L-valyl-N-[(1S)-1-[(4-chlorophenyl)methyl]-3,3,3-trifluoro-2-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



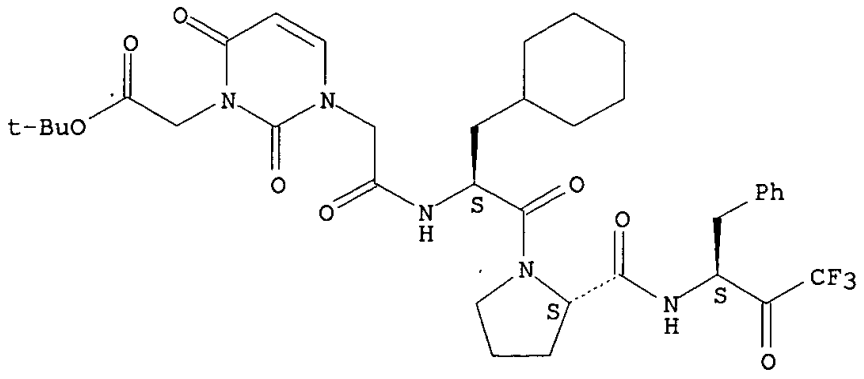
RN 402733-16-8 CAPLUS
CN L-Prolinamide, N-[[3-(carboxymethyl)-3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl]acetyl]-3-cyclohexyl-L-alanyl-N-[(1S)-3,3,3-trifluoro-2-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 402733-17-9 CAPLUS
CN L-Prolinamide, 3-cyclohexyl-N-[[3-[2-(1,1-dimethylethoxy)-2-oxoethyl]-3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl]acetyl]-L-alanyl-N-[(1S)-3,3,3-trifluoro-2-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



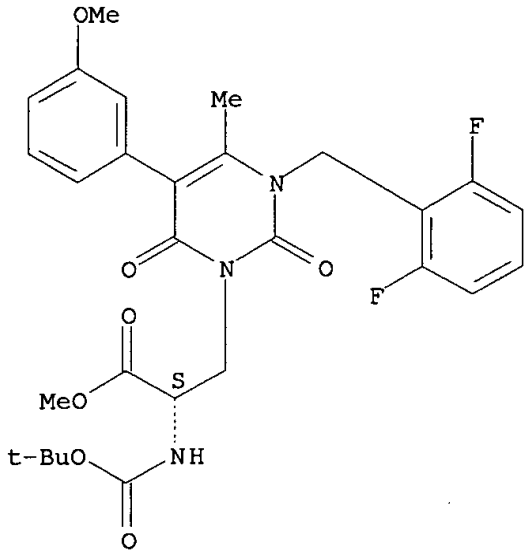
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 2001:565015 CAPLUS
DN 135:152816
TI Preparation of uracil derivatives as Gonadotropin-releasing hormone receptor antagonists
IN Zhu, Yun-Fei; Chen, Chen; Tucci, Fabio C.; Guo, Zhiqiang; Gross, Timothy D.; Rowbottom, Martin; Struthers, R. Scott
PA Neurocrine Biosciences, Inc., USA
SO PCT Int. Appl., 151 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001055119	A2	20010802	WO 2001-US2740	20010125
	WO 2001055119	A3	20020214		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2002132820	A1	20020919	US 2001-771107	20010125
	EP 1255738	A2	20021113	EP 2001-910362	20010125
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	NO 2002003525	A	20020724	NO 2002-3525	20020724
PRAI	US 2000-177933P	P	20000125		
	US 2000-239683P	P	20001011		
	WO 2001-US2740	W	20010125		

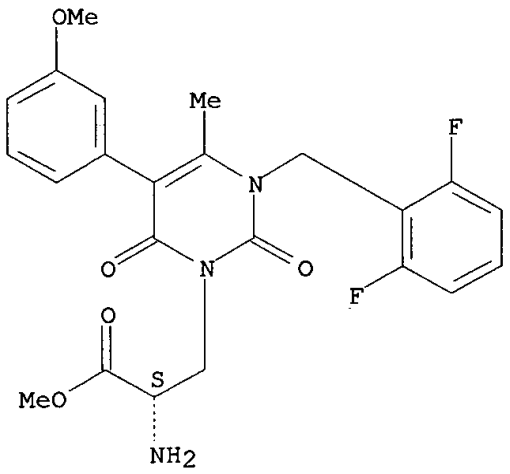
OS MARPAT 135:152816
AB Title compds. [I; R = arylalkyl; A = O, S, amino; R1 = alkyl, aryl, heterocycle; R2 = aryl, heterocycle, alkylaminocarbonyl, alkoxycarbonyl; R3 = alkylaminoalkyl, arylaminoalkyl, heterocyclylaminoalkyl, aminoalkyl, heterocyclylalkyl], stereoisomers, pharmaceutically acceptable salts, and prodrugs are prepd. Compns. contg. a I of this invention in combination with a pharmaceutically acceptable carrier, as well as methods relating to the use thereof for antagonizing gonadotropin-releasing hormone in both men and women are disclosed in the treatment of a variety of sex-hormone related conditions. Thus, the title compd. II was prepd. and biol. tested.
IT **352302-19-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of uracils as gonadotropin-releasing hormone receptor antagonists)
RN 352302-19-3 CAPLUS
CN 1(2H)-Pyrimidinepropanoic acid, 3-[(2,6-difluorophenyl)methyl]-.alpha.-[[(1,1-dimethylethoxy)carbonyl]amino]-3,6-dihydro-5-(3-methoxyphenyl)-4-methyl-2,6-dioxo-, methyl ester, (.alpha.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



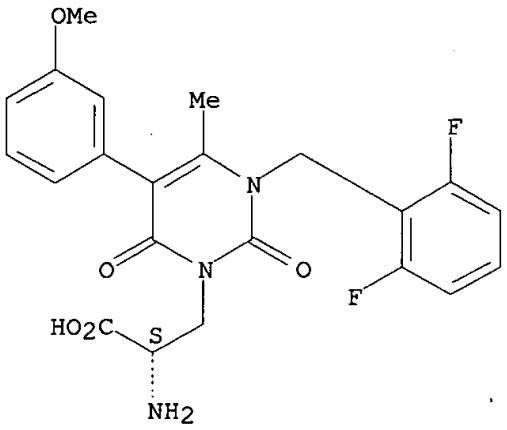
IT **352290-91-6P 352290-92-7P**
RL: SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of uracils as gonadotropin-releasing hormone receptor antagonists)
RN 352290-91-6 CAPLUS
CN 1(2H)-Pyrimidinepropanoic acid, .alpha.-amino-3-[(2,6-difluorophenyl)methyl]-3,6-dihydro-5-(3-methoxyphenyl)-4-methyl-2,6-dioxo-, methyl ester, (.alpha.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 352290-92-7 CAPLUS
CN 1(2H)-Pyrimidinepropanoic acid, .alpha.-amino-3-[(2,6-difluorophenyl)methyl]-3,6-dihydro-5-(3-methoxyphenyl)-4-methyl-2,6-dioxo-, (.alpha.S)- (9CI) (CA INDEX NAME)

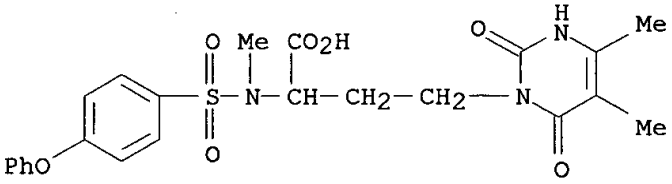
Absolute stereochemistry.


OMe
Me
F
N
O
N
O
F
HO2C
S
NH2

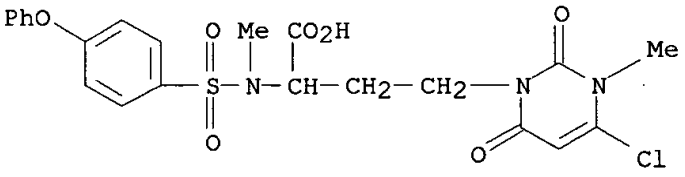
L21 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 2001:444501 CAPLUS
DN 135:56063
TI Sulfonamide derivatives as matrix metalloproteinase inhibitors
IN Kimura, Tomio; Miyazaki, Shojiro; Ueda, Keishi; Tanzawa, Kazuhiko; Ushiyama, Shigeru; Takasaki, Wataru
PA Sankyo Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 120 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2001163786	A2	20010619	JP 2000-297744	20000929
PRAI JP 1999-278300	A	19990930		

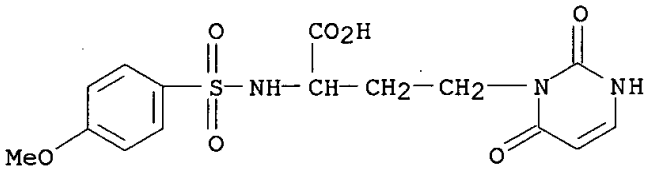
OS MARPAT 135:56063
AB The sulfonamide derivs. (I; R1 = H, NHOH; R2 = H, (substituted)alkyl, cycloalkyl, -AR6 [A = O, -S(O)m- or -n(R9)- with alkylene; R6 = other groups]; R3 = H, (substituted)-alkyl, -cycloalkyl, -alkenyl, and -alkynyl; R4 = (substituted)(hetero)arylene; R5 = (substituted)-alkyl and -(hetero)aryl) and their pharmacol. acceptable salts are claimed as matrix metalloproteinase inhibitors for treatment of arthritis, rheumatoid arthritis, cancer metastasis, and breast cancer.
IT **246263-03-6P 246263-58-1P 246263-80-9P 246263-87-6P 246263-91-2P 246264-19-7P 246264-41-5P 246264-44-8P 246264-63-1P 246264-64-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(sulfonamide derivs. as matrix metalloproteinase inhibitors)
RN 246263-03-6 CAPLUS
CN 1(2H)-Pyrimidinebutanoic acid, 3,6-dihydro-4,5-dimethyl-.alpha.-[methyl[(4-phenoxyphenyl)sulfonyl]amino]-2,6-dioxo- (9CI) (CA INDEX NAME)



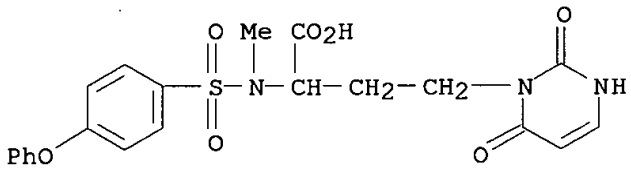
RN 246263-58-1 CAPLUS
CN 1(2H)-Pyrimidinebutanoic acid, 4-chloro-3,6-dihydro-3-methyl-.alpha.-[methyl[(4-phenoxyphenyl)sulfonyl]amino]-2,6-dioxo- (9CI) (CA INDEX NAME)



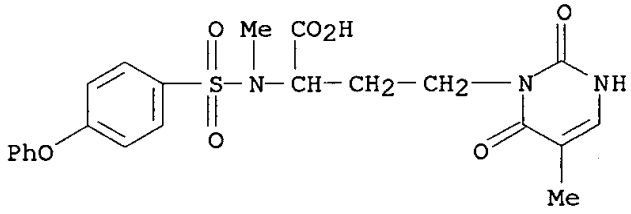
RN 246263-80-9 CAPLUS
CN 1(2H)-Pyrimidinebutanoic acid, 3,6-dihydro-.alpha.-[[(4-methoxyphenyl)sulfonyl]amino]-2,6-dioxo- (9CI) (CA INDEX NAME)



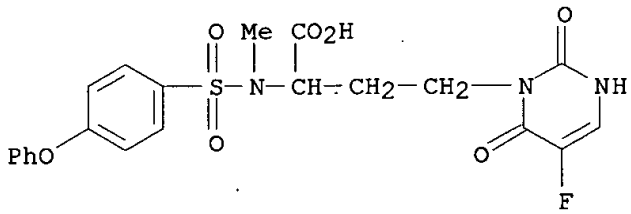
RN 246263-87-6 CAPLUS
CN 1(2H)-Pyrimidinebutanoic acid, 3,6-dihydro-.alpha.-[methyl[(4-phenoxyphenyl)sulfonyl]amino]-2,6-dioxo- (9CI) (CA INDEX NAME)



RN 246263-91-2 CAPLUS
CN 1(2H)-Pyrimidinebutanoic acid, 3,6-dihydro-5-methyl-.alpha.-[methyl[(4-phenoxyphenyl)sulfonyl]amino]-2,6-dioxo- (9CI) (CA INDEX NAME)

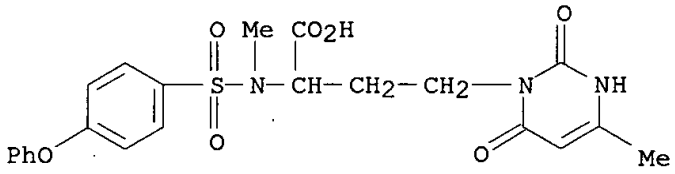


RN 246264-19-7 CAPLUS
CN 1(2H)-Pyrimidinebutanoic acid, 5-fluoro-3,6-dihydro-.alpha.-[methyl[(4-phenoxyphenyl)sulfonyl]amino]-2,6-dioxo- (9CI) (CA INDEX NAME)

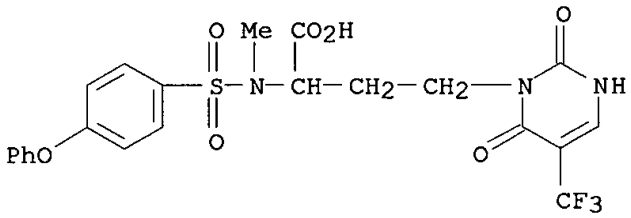


RN 246264-41-5 CAPLUS

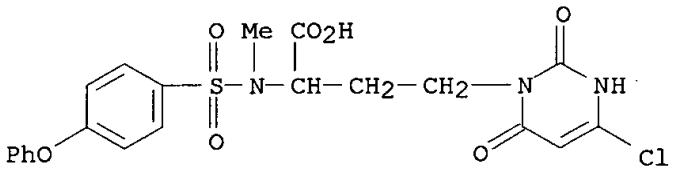
CN 1(2H)-Pyrimidinebutanoic acid, 3,6-dihydro-4-methyl-.alpha.-[methyl[(4-phenoxyphenyl)sulfonyl]amino]-2,6-dioxo- (9CI) (CA INDEX NAME)



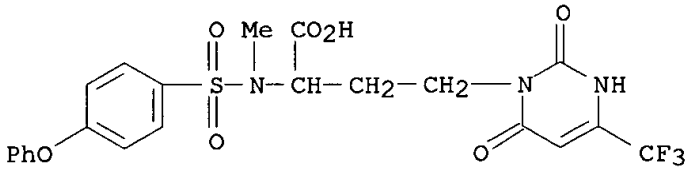
RN 246264-44-8 CAPLUS
CN 1(2H)-Pyrimidinebutanoic acid, 3,6-dihydro-.alpha.-[methyl[(4-phenoxyphenyl)sulfonyl]amino]-2,6-dioxo-5-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 246264-63-1 CAPLUS
CN 1(2H)-Pyrimidinebutanoic acid, 4-chloro-3,6-dihydro-.alpha.-[methyl[(4-phenoxyphenyl)sulfonyl]amino]-2,6-dioxo- (9CI) (CA INDEX NAME)



RN 246264-64-2 CAPLUS
CN 1(2H)-Pyrimidinebutanoic acid, 3,6-dihydro-.alpha.-[methyl[(4-phenoxyphenyl)sulfonyl]amino]-2,6-dioxo-4-(trifluoromethyl)- (9CI) (CA INDEX NAME)



L21 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 2000:628158 CAPLUS
DN 133:223051
TI Preparation of proline-containing peptides, intermediates thereof, and elastase inhibitors
IN Sato, Fuminori; Inoue, Yasunao; Omodani, Tomoki; Shiratake, Ryotaro; Honda, Seiji; Komiya, Masanobu; Takemura, Tadashi
PA Dainippon Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000052032	A1	20000908	WO 2000-JP1022	20000223
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
JP 2000256396	A2	20000919	JP 1999-56052	19990303
NZ 513594	A	20010928	NZ 2000-513594	20000223
EP 1157998	A1	20011128	EP 2000-905282	20000223
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000008600	A	20011226	BR 2000-8600	20000223
ZA 2001006514	A	20020510	ZA 2001-6514	20010808
PRAI JP 1999-56052	A	19990303		
WO 2000-JP1022	W	20000223		

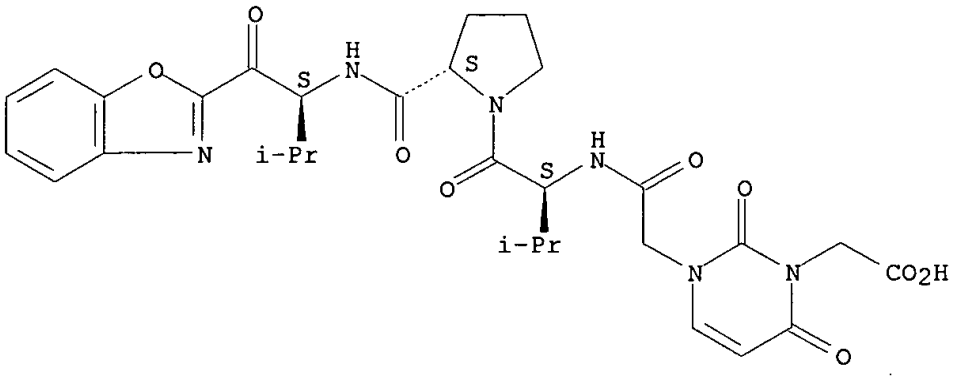
OS MARPAT 133:223051
AB Heterocyclic compds. represented by general formula [I; A, B = optionally oxo-substituted lower alkyl; D = mono- or bicyclic heterocyclic group Q; wherein D1 = optionally oxo-substituted CH2 or CH2CH2; ring G = (un)substituted 5-14 membered mono- or bicyclic (un)satd. heterocyclic ring; R1, R2 = lower alkyl; R3, R4 = H or OH, or R1 and R2 together represents oxo; R5 = (CX1X2)n(CH2)mY1; wherein X1, X2 = halo; Y1 = H, halo, lower alkoxycarbonyl, lower alkylaminocarbonyl, aralkylaminocarbonyl, aralkyloxycarbonyl, etc.], its esters or salts thereof are prepd. Also claimed is human neutrophilic elastase inhibitors contg. I as the active ingredient. Thus, oxidn. of 2-(3-tert-butoxycarbonylmethyl-2-oxo-1-imidazolidinyl)acetyl-L-valyl-N-[(1S,2S)-3,3,3-trifluoro-1-isopropyl-2-hydroxypropyl]-L-prolinamide with Dess-Martin reagent in CH2Cl2 at room temp. for 1 h, followed by treatment with CF3CO2H gave the title compd. (II; R = Q1, R5 = CF3) (III). III and II (R = Q2, R5 = benzoxazol-2-yl) showed IC50 of 0.010 and 0.005 .mu.g/mL against human neutrophilic elastase, resp. Pharmaceutical formulations contg. I were also prepd.
IT **291778-79-5P 291778-80-8P 291778-95-5P 291779-03-8P 291779-19-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of proline-contg. peptides, intermediates thereof, and elastase

inhibitors)

RN 291778-79-5 CAPLUS

CN L-Prolinamide, N-[[3-(carboxymethyl)-3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl]acetyl]-L-valyl-N-[(1S)-1-(2-benzoxazolylcarbonyl)-2-methylpropyl]- (9CI) (CA INDEX NAME)

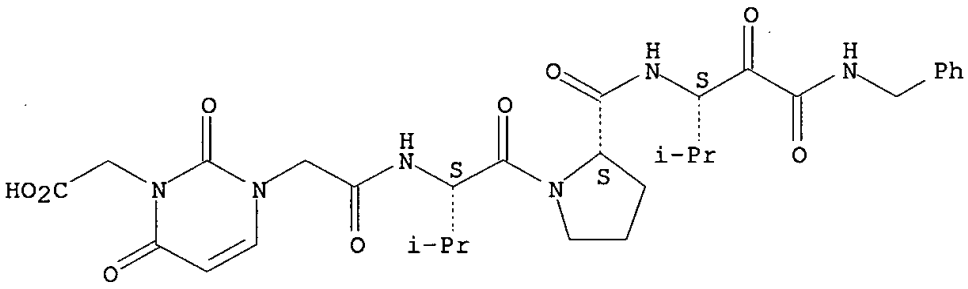
Absolute stereochemistry.



RN 291778-80-8 CAPLUS

CN L-Prolinamide, N-[[3-(carboxymethyl)-3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl]acetyl]-L-valyl-N-[(1S)-1-(1-methylethyl)-2,3-dioxo-3-[(phenylmethyl)amino]propyl]- (9CI) (CA INDEX NAME)

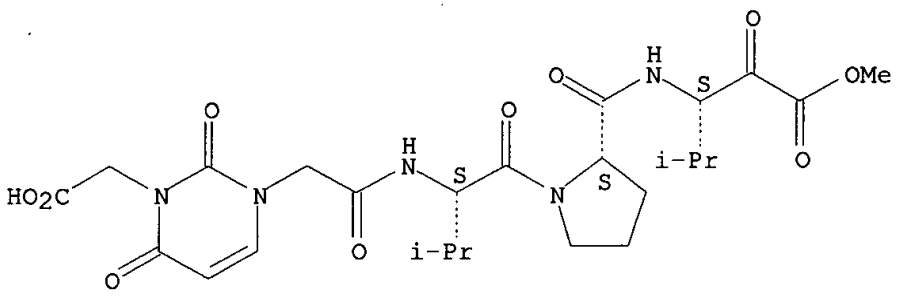
Absolute stereochemistry.



RN 291778-95-5 CAPLUS

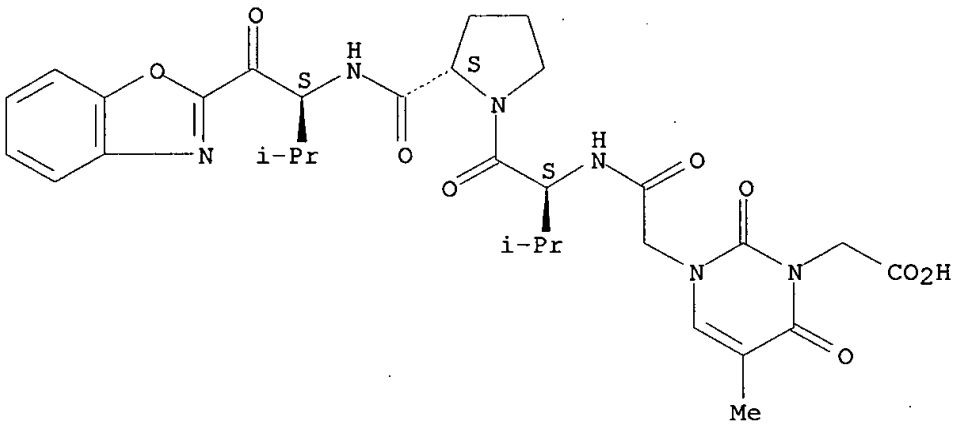
CN L-Prolinamide, N-[[3-(carboxymethyl)-3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl]acetyl]-L-valyl-N-[(1S)-3-methoxy-1-(1-methylethyl)-2,3-dioxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



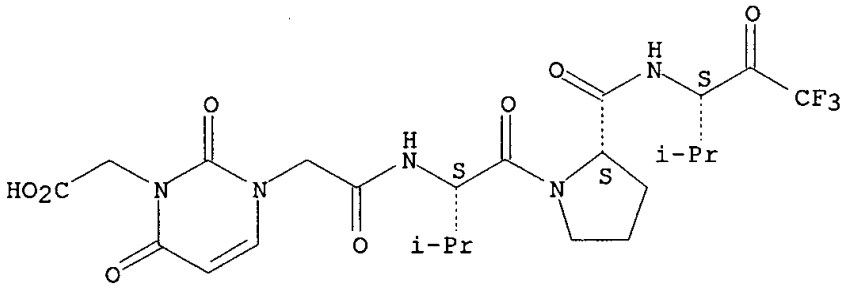
RN 291779-03-8 CAPLUS
CN L-Prolinamide, N-[[3-(carboxymethyl)-3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl]acetyl]-L-valyl-N-[(1S)-1-(2-benzoxazolylcarbonyl)-2-methylpropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 291779-19-6 CAPLUS
CN L-Prolinamide, N-[[3-(carboxymethyl)-3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl]acetyl]-L-valyl-N-[(1S)-3,3,3-trifluoro-1-(1-methylethyl)-2-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

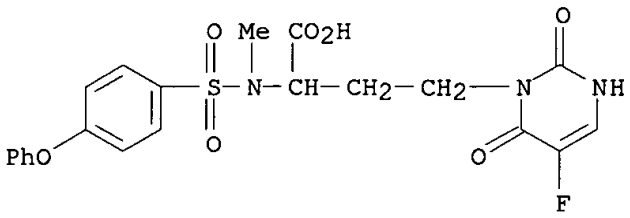


RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

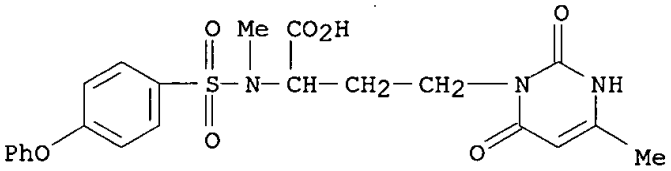
L21 ANSWER 8 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 1999:659358 CAPLUS
DN 131:286264
TI Preparation of phenylsulfonamide derivatives as proteinase and aggrecanase inhibitors
IN Kimura, Tomio; Miyazaki, Shoujiro; Ueda, Keiji; Tanzawa, Kazuhiko; Ushiyama, Shigeru; Takasaki, Wataru
PA Sankyo Company, Limited, Japan
SO PCT Int. Appl., 285 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9951572	A1	19991014	WO 1999-JP1751	19990402
	W: AU, BR, CA, CN, CZ, HU, ID, IL, IN, KR, MX, NO, NZ, PL, PT, RU, TR, US, ZA				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2327290	AA	19991014	CA 1999-2327290	19990402
	AU 9929615	A1	19991025	AU 1999-29615	19990402
	JP 2000319250	A2	20001121	JP 1999-96827	19990402
	BR 9909398	A	20001226	BR 1999-9398	19990402
	EP 1069110	A1	20010117	EP 1999-910822	19990402
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	NO 2000004949	A	20001107	NO 2000-4949	20001002
PRAI	JP 1998-91819	A	19980403		
	JP 1999-53164	A	19990301		
	WO 1999-JP1751	W	19990402		

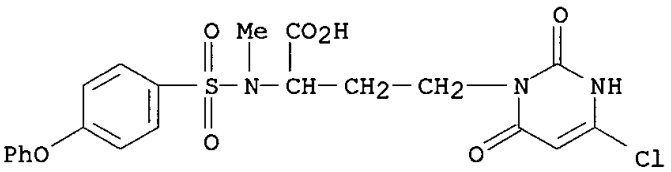
OS MARPAT 131:286264
AB Title compds. R5OR4SO2N(R3)CH(R2)COR1 [I; wherein R1 is H or NHOH; R2 is H, optionally substituted alkyl, cycloalkyl, or AR6 (wherein A is O, S(O)m, or alkylene optionally interrupted by N(R9); and R6 is a group represented by Q, Q1, Q2 wherein X is O, S, N(R10), or C(R11)(R12); Y is O, CO, S(O)n, N(R10), or C(R11)(R12); R7 and R8 each is H, alkyl, COOH, optionally substituted alkyl, etc.; R9, R10, R11, and R12 each is H, alkyl, etc.; and m and n each is 0 to 2); R3 is H, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted alkenyl, or optionally substituted alkynyl; R4 is optionally substituted (hetero)arylene; and R5 is optionally substituted alkyl or optionally substituted (hetero)aryl], stereoisomers, pharmacol. acceptable salts, esters, or other derivs. thereof are prepd. and tested as matrix metalloproteinase-13 inhibitors and aggrecanase inhibitors. Thus, the title compd. II was prepd.
IT **246264-19-7P 246264-41-5P 246264-63-1P 246264-64-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of phenylsulfonamides as proteinase and aggrecanase inhibitors)
RN 246264-19-7 CAPLUS
CN 1(2H)-Pyrimidinebutanoic acid, 5-fluoro-3,6-dihydro-.alpha.-[methyl[(4-phenoxyphenyl)sulfonyl]amino]-2,6-dioxo- (9CI) (CA INDEX NAME)



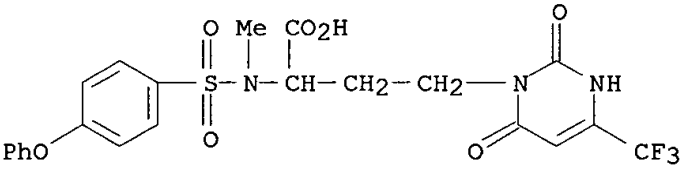
RN 246264-41-5 CAPLUS
CN 1(2H)-Pyrimidinebutanoic acid, 3,6-dihydro-4-methyl-.alpha.-[methyl[(4-phenoxyphenyl)sulfonyl]amino]-2,6-dioxo- (9CI) (CA INDEX NAME)



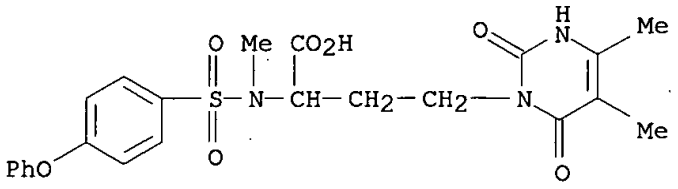
RN 246264-63-1 CAPLUS
CN 1(2H)-Pyrimidinebutanoic acid, 4-chloro-3,6-dihydro-.alpha.-[methyl[(4-phenoxyphenyl)sulfonyl]amino]-2,6-dioxo- (9CI) (CA INDEX NAME)



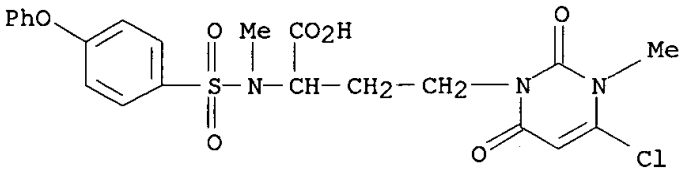
RN 246264-64-2 CAPLUS
CN 1(2H)-Pyrimidinebutanoic acid, 3,6-dihydro-.alpha.-[methyl[(4-phenoxyphenyl)sulfonyl]amino]-2,6-dioxo-4-(trifluoromethyl)- (9CI) (CA INDEX NAME)



IT **246263-03-6P 246263-58-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of phenylsulfonamides as proteinase and aggrecanase inhibitors)
RN 246263-03-6 CAPLUS
CN 1(2H)-Pyrimidinebutanoic acid, 3,6-dihydro-4,5-dimethyl-.alpha.-[methyl[(4-phenoxyphenyl)sulfonyl]amino]-2,6-dioxo- (9CI) (CA INDEX NAME)

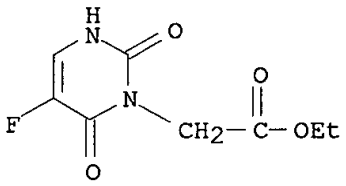


RN 246263-58-1 CAPLUS
CN 1(2H)-Pyrimidinebutanoic acid, 4-chloro-3,6-dihydro-3-methyl-.alpha.-[methyl[(4-phenoxyphenyl)sulfonyl]amino]-2,6-dioxo- (9CI) (CA INDEX NAME)



RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

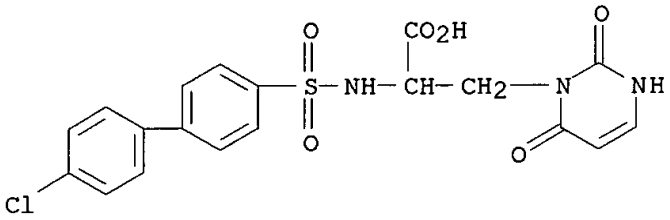
L21 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 1998:808504 CAPLUS
DN 130:261538
TI Synthesis of 5-fluorouracil derivatives and their antitumor activities
AU Sun, Changjun; Xue, Jun; Wang, Yigui; Zhang, Jiming; Qi, Yuxin; Li, Hongxiang
CS Department of Chemistry, Shandong University, Ji'nan, 250100, Peop. Rep. China
SO Zhongguo Yaowu Huaxue Zazhi (1998), 8(2), 91-95
CODEN: ZYHZEF; ISSN: 1005-0108
PB Zhongguo Yaowu Huaxue Zazhi Bianjibu
DT Journal
LA Chinese
AB A series of 2,3-disubstituted-5-fluoro-4-pyrimidinones were synthesized by the reaction of 2-O-alkyl-5-fluoro-3H-4-pyrimidinone with halogen compds. under phase transfer catalysis. Several 3-N-substituted-5-fluoro-1H-4-pyrimidinones were prepd. by the hydrogenation of 2-O-benzyl-3-N-substituted 5-fluoro-4-pyrimidinones in the presence of Pb-C catalyst. Their structures were confirmed by IR, 1H-NMR and MS. The preliminary antitumor tests showed that some of them had good antitumor activities.
IT **118004-33-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of 5-fluorouracil derivs. and their antitumor activities)
RN 118004-33-4 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 5-fluoro-3,6-dihydro-2,6-dioxo-, ethyl ester (9CI) (CA INDEX NAME)



L21 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 1998:742172 CAPLUS
DN 129:331057
TI Preparation and use of sulfonyldiaminocarboxylic acids as matrix-metalloproteinase inhibitors
IN Thorwart, Werner; Schwab, Wilfried; Schudok, Manfred; Haase, Burkhard; Neises, Bernhard; Billen, Gunter
PA Hoechst Aktiengesellschaft, Germany
SO Eur. Pat. Appl., 77 pp.
CODEN: EPXXDW
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 877019	A1	19981111	EP 1998-108040	19980502
	EP 877019	B1	20011212		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	DE 19719585	A1	19981112	DE 1997-19719585	19970509
	DE 19719428	A1	19981119	DE 1997-19719428	19970512
	AT 210639	E	20011215	AT 1998-108040	19980502
	ES 2165640	T3	20020316	ES 1998-108040	19980502
	CA 2237052	AA	19981109	CA 1998-2237052	19980507
	AU 9864824	A1	19981112	AU 1998-64824	19980508
	AU 736700	B2	20010802		
	CN 1205328	A	19990120	CN 1998-115265	19980508
	CN 1206001	A	19990127	CN 1998-109840	19980508
	BR 9801604	A	19990608	BR 1998-1604	19980508
	JP 11228529	A2	19990824	JP 1998-162707	19980508
	US 6159995	A	20001212	US 1998-74587	19980508
	US 6355673	B1	20020312	US 2000-690475	20001018
PRAI	DE 1997-19719585	A	19970509		
	DE 1997-19719428	A	19970512		
	US 1998-74587	A3	19980508		

OS MARPAT 129:331057
AB Title compds. [(I); R = (substituted)phenyl or heteroarom. group; R1 = H, (substituted)alkyl, 2-pyridinyl-methyl; R2, G independently = H, (substituted)alkyl, alkenyl, (substituted)phenyl; R2, G together = (substituted) ring; A = bond, O, CY:CY; Y = H, bond; B = (CH2)1-3, O(CH2)1-5, CH:CH, bond; D = (CH2)1-6, where one C may be replaced by NH, O, or S; X = CH:CH, O, S], useful as matrix-metalloproteinase inhibitors, were prepd. and tested. Thus, (R)-citrulline was reacted with Cl-4-C6H4-SO2Cl to give I [R = Cl-4-C6H4; R1,R2 = H; A,B = bond; D = (CH2)3; G = CONH2 (II)], in 54% yield. In in vitro fluorescence extinction tests with stromelysin and neutrophilic collagenase, II had IC50 of 50x10-9 Mol/l and 7x10-9 Mol/l resp.
IT **215164-80-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and use of sulfonyldiaminocarboxylic acids as matrix-metalloproteinase inhibitors)
RN 215164-80-0 CAPLUS
CN 1(2H)-Pyrimidinepropanoic acid, .alpha.-[[(4'-chloro[1,1'-biphenyl]-4-yl)sulfonyl]amino]-3,6-dihydro-2,6-dioxo- (9CI) (CA INDEX NAME)

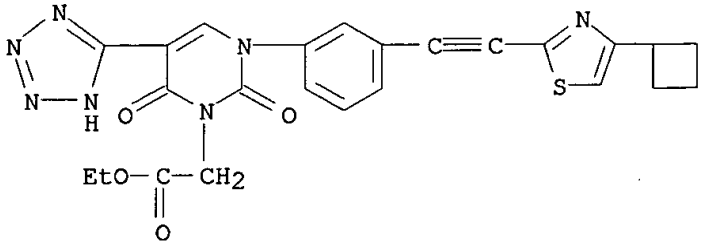


RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

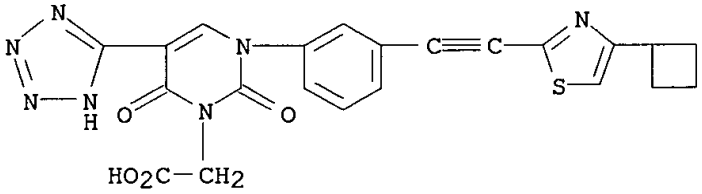
L21 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 1998:493329 CAPLUS
DN 129:189329
TI Preparation of 2-ethynylthiazole derivatives as leukotriene antagonists
IN Nakayama, Atsushi; Takeda, Satoshi; Machinaga, Nobuo; Ogasawara, Tomomi; Naito, Hiroshi; Hasegawa, Masashi; Haruda, Makoto
PA Daiichi Seiyaku Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 121 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 10195063	A2	19980728	JP 1997-286340	19971020
PRAI	JP 1996-278347		19961021		

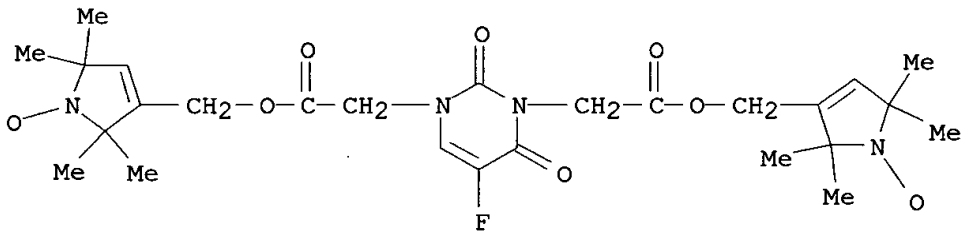
OS MARPAT 129:189329
AB The title compds. [I; R1, R2 = H, halo, (un)substituted alkyl or cycloalkyl; or R1 and R2 together form a ring; A = (un)substituted Ph, pyridyl, furyl, thienyl, benzofuranyl, benzo[b]thienyl, benzoxazolyl, benzothiazolyl, pyrido[1,2-a]pyrimidinyl, quinazolyl, benzotriazinyl, or 2H-chromenyl; G1 = O, CO, C.tplbond.C, (un)substituted NR3CO, NR4, NR5SO2, SO2NR6, CONR7, C(:CHR8), CR9:CR10; R3 - R7 = H, OH, (un)substituted alkyl; R8 = cyano, CO2H, (un)substituted alkoxycarbonyl; R9, R10 = H, halo, (un)substituted alkyl, cycloalkyl, or aryl; or R9 and R10 together form a ring; G2 = (un)substituted Ph, pyridyl, thiazolyl, isoxazolyl, thienyl, or pyrimidinyl, etc.; m, n = 0, 1; Q = CO2H, (un)substituted alkoxycarbonyl, 5-tetrazolylaminocarbonyl, (un)substituted 5-tetrazolyl, 1,2,3-triazolyl, 2,4-dioxothiazolidin-5-ylidene, or 4-oxo-2-thioxothiazolidin-5-ylidene, etc.; excluding the case where m = n = 0 and Q = CO2H or alkoxycarbonyl], which show photostability and activities of both leukotriene antagonism and inhibition of histamine release from mast cells, are prepd. A therapeutic or preventive drug contg. I as the active ingredient for the treatment of allergies or leukotriene and/or histamine-related diseases is claimed. Thus, 2-fluoro-4-[2-(4-methoxybenzyl)-2H-tetrazol-5-yl]benzoic acid was refluxed with SOCl2 in the presence of DMF in PhMe for 3 h and then condensed with 3-[2-(4-cyclobutyl-2-thiazolyl)ethynyl]aniline in the presence of Et3N, followed by treatment with anisole/CF3CO2H to give the title compd., ethynylthiazole contg. triazole deriv. (II). II in vitro showed IC50 5.7.times.10-10 M for inhibiting leukotriene D4-induced contraction of guinea pig's ileum and 9.3.times.10-9 M for inhibiting histamine release from rat's mast cells and in vivo inhibited leukotriene D4-induced contraction of guinea pig's air way with ID50 of 0.4 mg/kg p.o. An inhalant and capsule formulation contg. II were prepd.
IT **211938-99-7P 211939-00-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of ethynylthiazole derivs. as leukotriene antagonists for treatment of allergy and leukotriene and/or histamine-related diseases)
RN 211938-99-7 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 3-[3-[(4-cyclobutyl-2-thiazolyl)ethynyl]phenyl]-3,6-dihydro-2,6-dioxo-5-(1H-tetrazol-5-yl)-, ethyl ester (9CI) (CA INDEX NAME)



RN 211939-00-3 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 3-[3-[(4-cyclobutyl-2-thiazolyl)ethynyl]phenyl]-3,6-dihydro-2,6-dioxo-5-(1H-tetrazol-5-yl)-(9CI) (CA INDEX NAME)



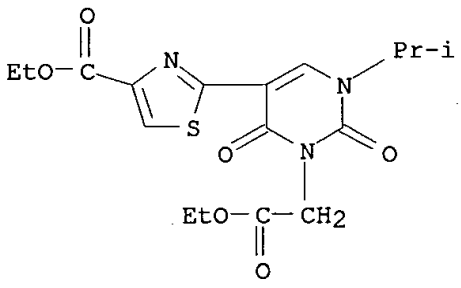
L21 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 1998:209563 CAPLUS
DN 128:261847
TI Syntheses and antitumor activities of spin-labeled 5-fluorouracil derivatives
AU Mao-Man-Jun; Tian, Xuan; Chen, Yao-Zu
CS Department Chemistry, Lanzhou University, Lanzhou, 730000, Peop. Rep. China
SO Gaodeng Xuexiao Huaxue Xuebao (1998), 19(3), 395-398
CODEN: KTHPDM; ISSN: 0251-0790
PB Gaodeng Jiaoyu Chubanshe
DT Journal
LA Chinese
AB Ten new spin-labeled derivs. of 5-fluorouracil were synthesized by introducing four kinds of stable nitroxyl radicals into N1 and N3 site of 5-Fu. The structures of these new compds. were confirmed by IR, UV, MS, ESR spectra and elemental anal. The antitumor activities of these compds. were tested to be against KB, HJCT-8 and A2780. The preliminary results showed that the antitumor activities of compds. 2a and 3a were stronger than that of 5-Fu and were similar to that of HCFU.
IT **205309-40-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(syntheses and antitumor activities of spin-labeled fluorouracil derivs.)
RN 205309-40-6 CAPLUS
CN 1H-Pyrrol-1-yloxy, 3,3'-[(5-fluoro-2,4-dioxo-1,3(2H,4H)-pyrimidinediyl)bis[(1-oxo-2,1-ethanediyl)oxymethylene]]bis[2,5-dihydro-2,2,5,5-tetramethyl- (9CI) (CA INDEX NAME)



L21 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 1997:732350 CAPLUS
DN 128:22760
TI Preparation of 5-thiazolyluracil derivatives as adenosine A3 receptor antagonists
IN Nakai, Eiichi; Kubota, Hideki; Tsuchiyama, Hirotaka
PA Yamanouchi Pharmaceutical Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 22 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 09291089	A2	19971111	JP 1996-107204	19960426
PRAI	JP 1996-107204		19960426		

OS MARPAT 128:22760
AB The derivs. I [R1-2 = H, (un)substituted lower alkyl, (un)substituted lower alkenyl, (un)substituted lower alkynyl, (un)crosslinked cycloalkyl; R3-4 = H, (un)substituted lower alkyl, carboxy, lower alkoxycarbonyl, lower acyl, carbamoyl, mono- or di(lower alkyl)carbamoyl] or their pharmaceutically acceptable salts are claimed. I are useful for treatment of disorders, in which mast cell degranulation is involved, e.g. ischemic diseases, allergic diseases, inflammatory diseases, etc. Also claimed are pharmaceuticals and adenosine A3 receptor antagonists contg. I or their salts as active ingredients. I were specifically bound to adenosine A3 receptors expressed on cell membrane of CHO-K1 cell transformed with a vector bearing human adenosine A3 receptor cDNA. Procedures for the prepn. of I (R1 = CH2Ph, R2 = Me, R3 = CO2Et, R4 = H), etc. were also provided. Pharmaceutical formulations contg. I were also given.
IT **199332-10-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of thiazolyluracil derivs. as adenosine A3 receptor antagonists)
RN 199332-10-0 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 5-[4-(ethoxycarbonyl)-2-thiazolyl]-3,6-dihydro-3-(1-methylethyl)-2,6-dioxo-, ethyl ester (9CI) (CA INDEX NAME)



L21 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 1997:541856 CAPLUS
DN 127:234613
TI Aromatic heterocyclic derivatives as enzyme inhibitors
IN Tamura, Susan Yoshiko; Semple, Joseph Edward; Ripka, William Charles; Ardecky, Robert John; Ge, Yu; Carpenter, Stephen H.; Brunck, Terence K.
PA Corvas International, Inc., USA
SO U.S., 65 pp., ont.-in-part of U.S. Ser. No. 356,833.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 7

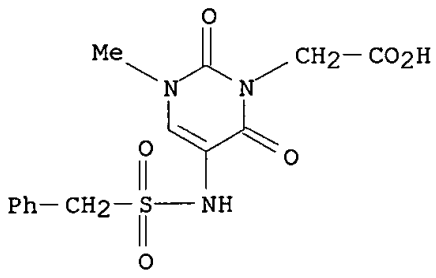
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5656645	A	19970812	US 1995-484506	19950607
CA 2206400	AA	19960620	CA 1995-2206400	19951213
WO 9618644	A1	19960620	WO 1995-US16410	19951213
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9644248	A1	19960703	AU 1996-44248	19951213
AU 693636	B2	19980702		
EP 804464	A1	19971105	EP 1995-943130	19951213
EP 804464	B1	20020508		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV				
BR 9509994	A	19971230	BR 1995-9994	19951213
CN 1169730	A	19980107	CN 1995-196753	19951213
JP 10510539	T2	19981013	JP 1995-519290	19951213
NZ 298699	A	20010330	NZ 1995-298699	19951213
AT 217321	E	20020515	AT 1995-943130	19951213
US 6008351	A	19991228	US 1995-573775	19951218
US 6011158	A	20000104	US 1996-659983	19960607
HU 77888	A2	19951213	HU 1998-1160	19980928
US 6342504	B1	20020129	US 1999-194855	19991221
PRAI US 1994-356833	A2	19941213		
US 1995-481660	A	19950607		
US 1995-484506	A	19950607		
WO 1995-US16410	W	19951213		
US 1995-573775	A2	19951218		
US 1996-659983	A2	19960607		
WO 1997-US9818	W	19970609		

OS MARPAT 127:234613
AB Heterocyclic arom. peptide aldehydes R1-X-NH-Het-CHR2CONHCH(CH2R3)CHO [Het = substituted 2-oxo-1-pyridyl, 6-oxo- or 2,6-dioxo-1-pyrimidinyl; R1 = (un)substituted alkyl, cycloalkyl, heterocyclyl, alkenyl, aryl, heteroaryl; R2 = H, alkyl, alkenyl; R3 = H2NC(:NH)NHCH2CH2; X = SO2, NR4SO2 (R4 = H, alkyl, aryl, aralkyl), CO, OCO, NHCO, P(O)R5 (R5 = NR4, OR4, R4, SR4, where R4 .noteq. H), or a direct bond] were prepd. as thrombin inhibitors. Thus, [3-[(benzylsulfonyl)amino]-2-oxo-1,2-dihydropyridyl]acetyl-L-argininal trifluoroacetate was prepd. by a multistep procedure and assayed for inhibition of human alpha-thrombin amidolytic activity (Ki = 289 .+-. 32 pM).
IT **179524-01-7P**

RL: SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of arom. peptide aldehydes as thrombin inhibitors)

RN 179524-01-7 CAPLUS

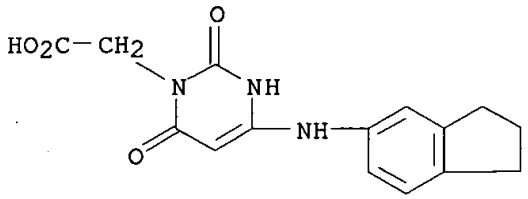
CN 1(2H)-Pyrimidineacetic acid, 3,6-dihydro-3-methyl-2,6-dioxo-5-[[(phenylmethyl)sulfonyl]amino]- (9CI) (CA INDEX NAME)



L21 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 1996:367740 CAPLUS
DN 125:26236
TI Novel antibiotic compounds and methods to treat gram-positive bacteria and mycoplasma infections
IN Brown, Neal C.; Wright, George
PA University of Massachusetts Medical Center, USA
SO PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9606614	A1	19960307	WO 1995-US10943	19950830
	W: AU, BG, BR, CA, CN, CZ, FI, HU, IS, JP, KP, KR, MX, NO, NZ, PL, RO, RU, SD, SG, UA, VN				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5516905	A	19960514	US 1994-298011	19940830
	CA 2198739	AA	19960307	CA 1995-2198739	19950830
	AU 9534185	A1	19960322	AU 1995-34185	19950830
	AU 703511	B2	19990325		
	EP 772439	A1	19970514	EP 1995-930997	19950830
	EP 772439	B1	20001004		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	JP 10509134	T2	19980908	JP 1995-508925	19950830
	AT 196735	E	20001015	AT 1995-930997	19950830
	ES 2151608	T3	20010101	ES 1995-930997	19950830
	AU 9935782	A1	19990909	AU 1999-35782	19990622
PRAI	US 1994-298011	A	19940830		
	AU 1995-34185	A3	19950830		
	WO 1995-US10943	W	19950830		

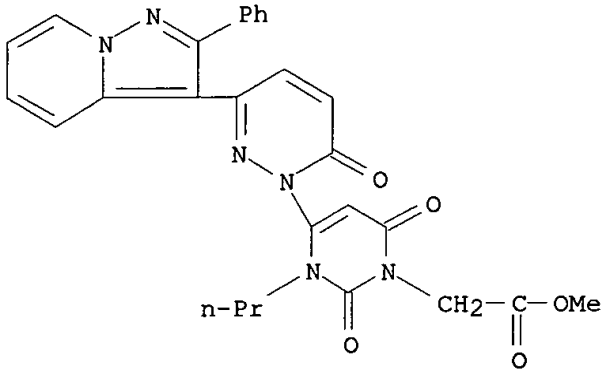
OS MARPAT 125:26236
AB A method of inhibiting replication of mycoplasma and gram-pos. bacteria is described. Useful new compds. for in vivo and in vitro inhibition and therapy for infections utilizing HPUra-like compds. are also provided. These include a no. of novel 3-substituted uracil and isocytosine compds., and 10-substituted guanine and adenine compds. The compds. inhibit the activity of DNA polymerase III. Twenty compds. such as 3-(2-hydroxyethyl)-6-(5-indanylamino)uracil are claimed.
IT **177792-96-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(antibiotic compds. for treatment of gram-pos. bacteria and mycoplasma infections)
RN 177792-96-0 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 4-[(2,3-dihydro-1H-inden-5-yl)amino]-3,6-dihydro-2,6-dioxo- (9CI) (CA INDEX NAME)


HO2C—CH2
O
N
NH
NH
O

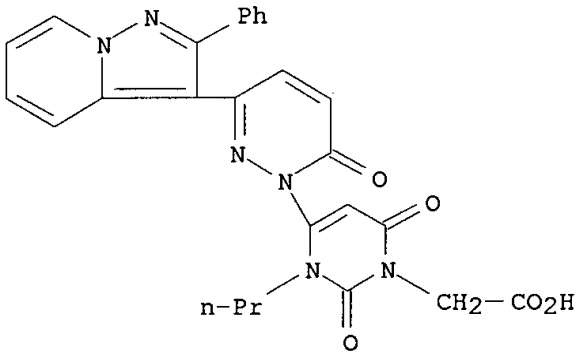
L21 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 1995:960198 CAPLUS
DN 124:8834
TI Preparation of (oxopyridazinyl)pyrazolopyridines as adenosine antagonists
IN Akahane, Atsushi; Nishimura, Shintaro; Itani, Hiromichi; Durkin, Kieran P. M.
PA Fujisawa Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 167 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9518128	A1	19950706	WO 1994-JP2230	19941226
	W: AU, CA, CN, FI, HU, JP, KR, NO, RU, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2180253	AA	19950706	CA 1994-2180253	19941226
	AU 9512817	A1	19950717	AU 1995-12817	19941226
	AU 694157	B2	19980716		
	EP 737193	A1	19961016	EP 1995-903969	19941226
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	CN 1139928	A	19970108	CN 1994-194724	19941226
	CN 1046724	B	19991124		
	HU 76280	A2	19970728	HU 1996-1789	19941226
	JP 09507485	T2	19970729	JP 1994-517911	19941226
	ZA 9410409	A	19950926	ZA 1994-10409	19941229
	IL 112193	A1	20001031	IL 1994-112193	19941229
	BR 9500905	A	19951024	BR 1995-905	19950306
	US 5773530	A	19980630	US 1996-663119	19960913
	US 6355640	B1	20020312	US 1998-72696	19980506
PRAI	GB 1993-26524	A	19931229		
	GB 1994-4323	A	19940304		
	WO 1994-JP2230	W	19941226		
	US 1996-663119	A1	19960913		

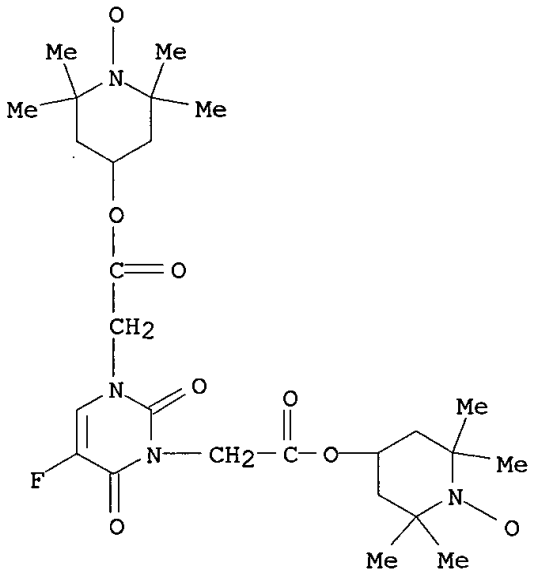
OS MARPAT 124:8834
AB Title compds. [I; R1 = aryl; R2 = (un)substituted cycloalkyl] were prepd. Thus, I (R1 = Ph, R2 = H) was alkylated by 2-chlorocyclohexanone and the product condensed with (EtO)2P(O)CH2CO2Et to give, after sapon., title compd. II and the exo-unsatd. product. II gave redn. of serum creatinine from 3.60 (control) to 1.10mg/dL i.v. in rats experiencing cisplatin-induced renal failure.
IT **171050-69-4P 171050-91-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of (oxopyridazinyl)pyrazolopyridines as adenosine antagonists)
RN 171050-69-4 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 3,6-dihydro-2,6-dioxo-4-[6-oxo-3-(2-phenylpyrazolo[1,5-a]pyridin-3-yl)-1(6H)-pyridazinyl]-3-propyl-, methyl ester (9CI) (CA INDEX NAME)



RN 171050-91-2 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 3,6-dihydro-2,6-dioxo-4-[6-oxo-3-(2-phenylpyrazolo[1,5-a]pyridin-3-yl)-1(6H)-pyridazinyl]-3-propyl- (9CI) (CA INDEX NAME)



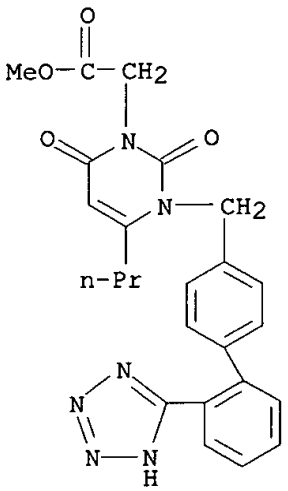
L21 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 1993:517198 CAPLUS
DN 119:117198
TI Synthesis of spin-labeled anticancer derivatives of 5-fluorouracil
AU Wang, Yanguang; Tian, Xuan; Li, Jingxin; Chen, Yaozu
CS Dep. Chem., Tianjin Univ., Tianjin, 300072, Peop. Rep. China
SO Gaodeng Xuexiao Huaxue Xuebao (1992), 13(12), 1561-3
CODEN: KTHPDM; ISSN: 0251-0790
DT Journal
LA Chinese
AB Ten spin-labeled derivs. of 5-fluorouracil were prepd. as the potential anticancer agents. The structures of these new compds. were examd. by IR, UV, mass spectra, ESR and elementary anal. The preliminary pharmacol. tests show that some of the compds. e.g., I and II possess anticancer activity against leukemia L1210 and uterine cervix carcinoma U14 in mice.
IT **149387-14-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and anticancer activity of)
RN 149387-14-4 CAPLUS
CN 1-Piperidinyloxy, 4,4'-[(5-fluoro-2,4-dioxo-1,3(2H,4H)-pyrimidinediyl)bis[(1-oxo-2,1-ethanediyl)oxy]]bis[2,2,6,6-tetramethyl-(9CI) (CA INDEX NAME)



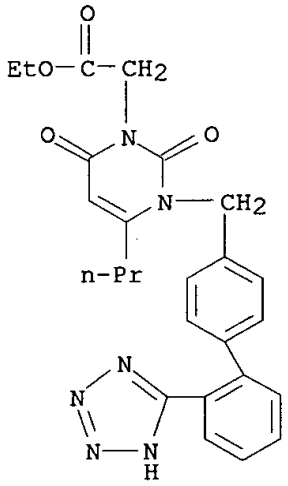
L21 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 1991:632277 CAPLUS
DN 115:232277
TI Preparation of 1-(tetrazolylbiphenylylmethyl)-2,4-pyrimidinediones as angiotensin II antagonists
IN Naka, Takehiko; Nishikawa, Kohei
PA Takeda Chemical Industries, Ltd., Japan
SO Eur. Pat. Appl., 39 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 442473	A1	19910821	EP 1991-102020	19910213
	EP 442473	B1	19980819		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	CA 2036304	AA	19910816	CA 1991-2036304	19910213
	CA 2036304	C	20010417		
	US 5162326	A	19921110	US 1991-654490	19910213
	AT 169915	E	19980915	AT 1991-102020	19910213
	JP 04330072	A2	19921118	JP 1991-20603	19910214
	JP 3032844	B2	20000417		
PRAI	JP 1990-34919	A	19900215		

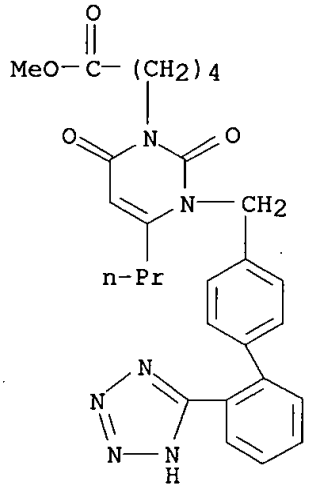
OS MARPAT 115:232277
AB Title compds. [I; R1 = H, (substituted) hydrocarbyl; R2 = H, halo, NO2, amino, CHO, (substituted) hydrocarbyl; R3 = (substituted) hdyrocarbyl; R4 = H, halo, NO2; R5 = residue capable of forming an anion or convertible to an anion; X = bond or spacer contg. O, N, S; Y = bond, spacer; n = 1,2], were prepd. Thus, 6-chloro-3-propylpyrimidine-2,4(1H, 3H)-dione was condensed with N-triphenylmethyl-5-[2-(4'-bromomethylbiphenyl)]tetrazole in DMF contg K2CO3 to give 67% coupling product, which was refluxed with PrSH and K2CO3 in MeCN to give 56% title compd. II. II inhibited binding of angiotensin II (A II) to AII receptors from bovine adrenal cortex with IC50 = 0.02 .mu.M. Several I at 30 mg/kg orally in rats inhibited the pressor action of AII by .gtoreq.70%. Dosage formulations were prepd. contg. II.
IT **137016-12-7P 137016-13-8P 137016-14-9P 137016-21-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as angiotensin II antagonist)
RN 137016-12-7 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 3,6-dihydro-2,6-dioxo-4-propyl-3-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)



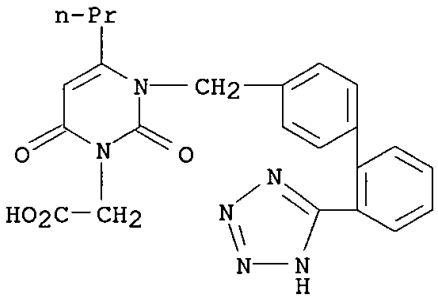
RN 137016-13-8 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 3,6-dihydro-2,6-dioxo-4-propyl-3-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, ethyl ester (9CI) (CA INDEX NAME)



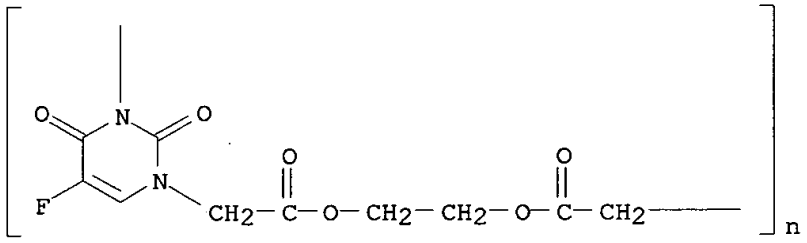
RN 137016-14-9 CAPLUS
CN 1(2H)-Pyrimidinepentanoic acid, 3,6-dihydro-2,6-dioxo-4-propyl-3-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, methyl ester (9CI) (CA INDEX NAME)



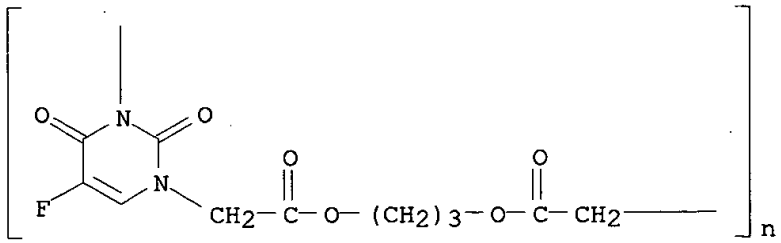
RN 137016-21-8 CAPLUS
CN 1(2H)-Pyrimidineacetic acid, 3,6-dihydro-2,6-dioxo-4-propyl-3-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]- (9CI) (CA INDEX NAME)



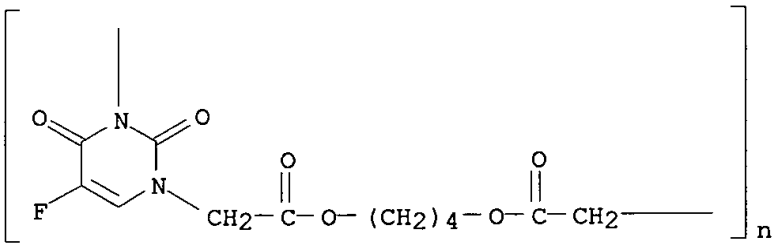
L21 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 1984:203210 CAPLUS
DN 100:203210
TI Chemotherapeutic polymers. II. Synthesis of polyesters containing 5-fluorouracil in the main chain
AU Zhuo, Renxi; Chen, Qusheng; Liu, Gaowei; Liu, Zhenhua; Wang, Xuan
CS Dep. Chem., Wuhan Univ., Wuhan, Peop. Rep. China
SO Gaofenzi Tongxun (1984), (1), 11-15
CODEN: KFTTAR; ISSN: 0453-2880
DT Journal
LA Chinese
AB Six new 5-fluorouracil (5-FU)-contg. polyesters, I (n = 2, 3, 4, 5, 6, and 10) were prepd. by reacting 5-FU [51-21-8] with bis-(.alpha.-chloroacetoxy)polymethylenes (n = 2, 3, 4, 5, 6, and 10). I.p. or orally injected I (n = 2) at dosages of 130-154 mg/kg showed 24.0-24.88% antisarcoma effect in mouse with S180 sarcoma; the antisarcoma effect of I (n = 2) was lower than that of 5-FU, but its toxicity was much less than that of 5-FU.
IT **90077-01-3P 90077-02-4P 90077-03-5P**
90077-04-6P 90077-05-7P 90077-06-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as neoplasm inhibitor)
RN 90077-01-3 CAPLUS
CN Poly[(5-fluoro-2,6-dioxo-1,3(2H,6H)-pyrimidinediyl)(2-oxo-1,2-ethanediyl)oxy-1,2-ethanediyloxy(1-oxo-1,2-ethanediyl)] (9CI) (CA INDEX NAME)



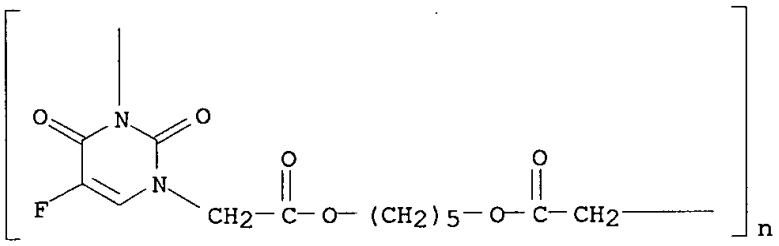
RN 90077-02-4 CAPLUS
CN Poly[(5-fluoro-2,6-dioxo-1,3(2H,6H)-pyrimidinediyl)(2-oxo-1,2-ethanediyl)oxy-1,3-propanediyloxy(1-oxo-1,2-ethanediyl)] (9CI) (CA INDEX NAME)



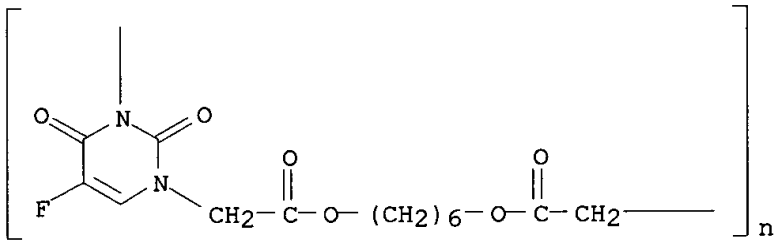
RN 90077-03-5 CAPLUS
CN Poly[(5-fluoro-2,6-dioxo-1,3(2H,6H)pyrimidinediyl)(2-oxo-1,2-ethanediyl)oxy-1,4-butanediyloxy(1-oxo-1,2-ethanediyl)] (9CI) (CA INDEX NAME)



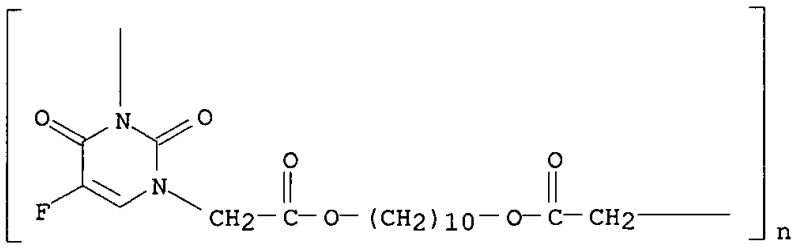
RN 90077-04-6 CAPLUS
CN Poly[(5-fluoro-2,6-dioxo-1,3(2H,6H)pyrimidinediyl)(2-oxo-1,2-ethanediyl)oxy-1,5-pentanediyloxy(1-oxo-1,2-ethanediyl)] (9CI) (CA INDEX NAME)



RN 90077-05-7 CAPLUS
CN Poly[(5-fluoro-2,6-dioxo-1,3(2H,6H)-pyrimidinediyl)(2-oxo-1,2-ethanediyl)oxy-1,6-hexanediyloxy(1-oxo-1,2-ethanediyl)] (9CI) (CA INDEX NAME)



RN 90077-06-8 CAPLUS
CN Poly[(5-fluoro-2,6-dioxo-1,3(2H,6H)-pyrimidinediyl)(2-oxo-1,2-ethanediyl)oxy-1,10-decanediyloxy(1-oxo-1,2-ethanediyl)] (9CI) (CA INDEX NAME)



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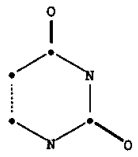

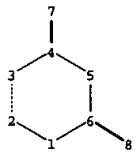

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ring bonds :
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exact/norm bonds :
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Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS

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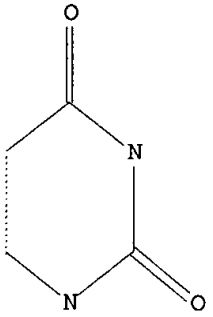


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                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:       263444 TO   277356
PROJECTED ANSWERS:          239693 TO   252975

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=> s l4 and l5
L6           63 L4 AND L5
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=> s convul?
L7       21745 CONVUL?

=> s l4 and l7
L8        1642 L4 AND L7

=> s treat? or therap?
       2871588 TREAT?
        321970 THERAP?
L9     3042475 TREAT? OR THERAP?

=> s l9(p)l7
L10       4089 L9(P)L7

=> s l4 and l10
L11        336 L4 AND L10

=> s inhibit?
L12    1563686 INHIBIT?

=> s l6 and l12
L13         23 L6 AND L12

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L13 ANSWER 1 OF 23 CAPLUS COPYRIGHT 2003 ACS
AN 2002:814111 CAPLUS
DN 137:325426
TI Preparation of pyrimidine derivatives as anti-ictogenic and/or anti-**epileptogenic** agents
IN Weaver, Donald F.; Guillain, Buhendwa Musole; Carran, John R.; Jones, Kathryn
PA Queen's University At Kingston, Can.
SO PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002083651	A2	20021024	WO 2002-CA512	20020411
WO 2002083651	A3	20021219		

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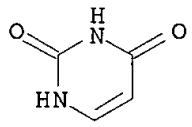
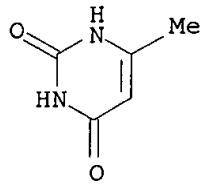
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

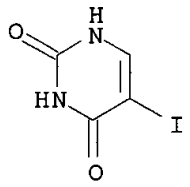
PRAI US 2001-282987P P 20010411
US 2001-285940P P 20010423
US 2001-310748P P 20010807
US 2002-99934 A 20020313
OS MARPAT 137:325426
AB Title compds., e.g., I [R9 = H, alkyl, alkynyl, aryl, amino, etc.; R10 = H, alkyl, aryl, carboxyl, etc.; R11 = H, alkyl, amino, thioether, tetrahydrofuranyl] and derivs. thereof were prepd. For instance, 5-hydroxymethyuracil (II) was prepd. from uracil and formaldehyde (KOHaq, 50.degree., 72 h). II and other example compds. tested were active in the hippocampal kindling seizure model. I are useful for the **inhibition** of convulsive disorders including epilepsy.
IT **66-22-8P**, 2,4(1H,3H)-Pyrimidinedione, preparation
626-48-2P 696-07-1P 140914-91-6P
153865-87-3P 473450-59-8P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of pyrimidine (uracil) derivs. as antiepileptic agents)
RN 66-22-8 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione (9CI) (CA INDEX NAME)



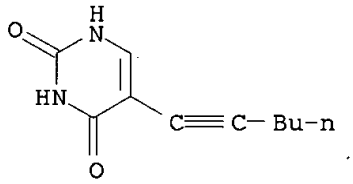
RN 626-48-2 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 6-methyl- (9CI) (CA INDEX NAME)



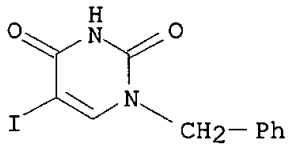
RN 696-07-1 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 5-iodo- (9CI) (CA INDEX NAME)



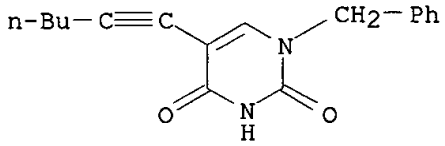
RN 140914-91-6 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 5-(1-hexynyl)- (9CI) (CA INDEX NAME)



RN 153865-87-3 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 5-iodo-1-(phenylmethyl)- (9CI) (CA INDEX NAME)

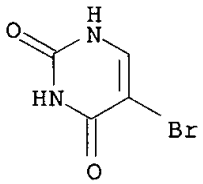


RN 473450-59-8 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 5-(1-hexynyl)-1-(phenylmethyl)- (9CI) (CA INDEX NAME)

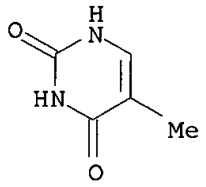


IT **51-20-7P 65-71-4P 65-86-1P,** 2,6-Dioxo-1,2,3,6-tetrahydropyrimidine-4-carboxylic acid **69-89-6P**, 3,9-Dihydropurine-2,6-dione **86-96-4P,** 2,4(1H,3H)-Quinazolinedione **615-77-0P 717-00-0P 874-14-6P 4433-40-3P 4874-40-2P,** 5-((Methylsulfanyl)methyl)-1H-pyrimidine-2,4-dione **6300-95-4P,** 6-Phenyldihydropyrimidine-2,4-dione **7164-43-4P,** 5-Amino-2,6-dioxo-1,2,3,6-tetrahydropyrimidine-4-carboxylic acid **15018-56-1P,** 5-Bromo-6-methyl-1H-pyrimidine-2,4-dione **16632-21-6P,** 6-Methyl-5-nitro-1H-pyrimidine-2,4-dione **20636-41-3P 23945-44-0P,** 2,4-Dioxo-11,2,3,4-tetrahydropyrimidine-5-carboxylic acid **26305-13-5P 33443-58-2P,** 1-Benzyl-6-methyl-1H-pyrimidine-2,4-dione **41613-26-7P,** 1,3-Dimethyl-5-nitro-1H-pyrimidine-2,4-dione **57712-64-8P,** 5-Bromo-1-isopropyl-1H-pyrimidine-2,4-dione **57712-66-0P,** 5-Bromo-1-sec-butyl-1H-pyrimidine-2,4-dione **57712-67-1P,** 1-Benzyl-5-bromo-1H-pyrimidine-2,4-dione **116371-83-6P,** 1,3-Bis(3-hydroxypropyl)-1H-pyrimidine-2,4-dione **137121-87-0P 200279-12-5P 473450-42-9P,** 5-Bromo-1-cyclohexylmethyl-1H-pyrimidine-2,4-dione **473450-45-2P,** 5-Bromo-1,3-bis((cyclohexyl)methyl)-1H-pyrimidine-2,4-dione **473450-48-5P,** 5-Bromo-1,3-bis(4-nitrobenzyl)-1H-pyrimidine-2,4-dione **473450-56-5P 473450-70-3P,** 6-Methyl-1,3-bis(4-nitrobenzyl)-1H-pyrimidine-2,4-dione **473450-79-2P 473450-82-7P,** 3-Amino-1-benzyldihydropyrimidine-2,4-dione **473450-83-8P,** 3-Amino-1-benzyl-6-methyldihydropyrimidine-2,4-dione **473450-84-9P,** 6-m-Tolyldihydropyrimidine-2,4-dione **473450-86-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pyrimidine (uracil) derivs. as antiepileptic agents)

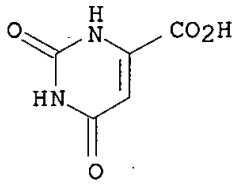
RN 51-20-7 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 5-bromo- (9CI) (CA INDEX NAME)



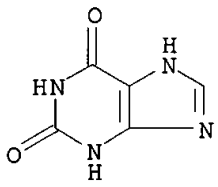
RN 65-71-4 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 5-methyl- (9CI) (CA INDEX NAME)



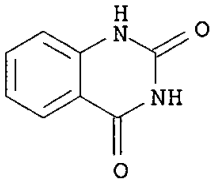
RN 65-86-1 CAPLUS
CN 4-Pyrimidinecarboxylic acid, 1,2,3,6-tetrahydro-2,6-dioxo- (9CI) (CA INDEX NAME)



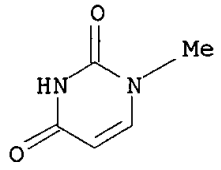
RN 69-89-6 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro- (9CI) (CA INDEX NAME)



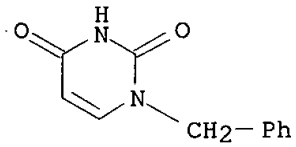
RN 86-96-4 CAPLUS
CN 2,4(1H,3H)-Quinazolinedione (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



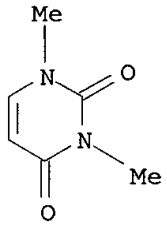
RN 615-77-0 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-methyl- (9CI) (CA INDEX NAME)



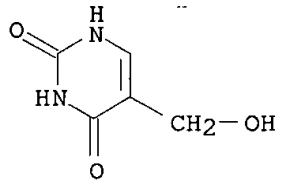
RN 717-00-0 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-(phenylmethyl)- (9CI) (CA INDEX NAME)



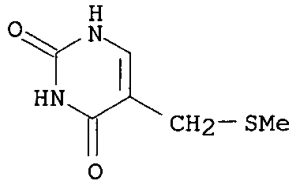
RN 874-14-6 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1,3-dimethyl- (9CI) (CA INDEX NAME)



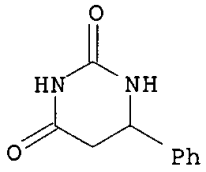
RN 4433-40-3 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 5-(hydroxymethyl)- (9CI) (CA INDEX NAME)



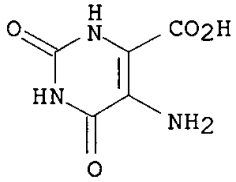
RN 4874-40-2 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 5-[(methylthio)methyl]- (9CI) (CA INDEX NAME)



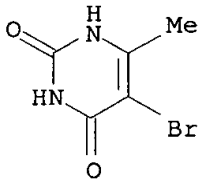
RN 6300-95-4 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, dihydro-6-phenyl- (9CI) (CA INDEX NAME)



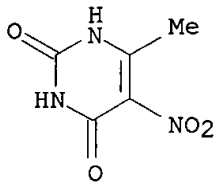
RN 7164-43-4 CAPLUS
CN 4-Pyrimidinecarboxylic acid, 5-amino-1,2,3,6-tetrahydro-2,6-dioxo- (9CI) (CA INDEX NAME)



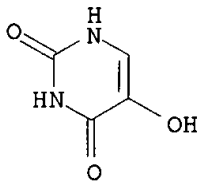
RN 15018-56-1 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 5-bromo-6-methyl- (9CI) (CA INDEX NAME)



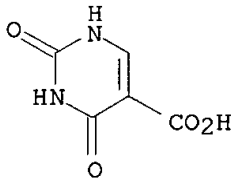
RN 16632-21-6 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 6-methyl-5-nitro- (9CI) (CA INDEX NAME)



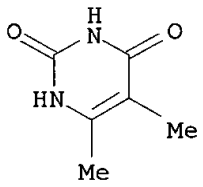
RN 20636-41-3 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 5-hydroxy- (9CI) (CA INDEX NAME)



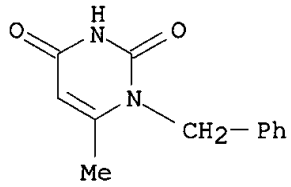
RN 23945-44-0 CAPLUS
CN 5-Pyrimidinecarboxylic acid, 1,2,3,4-tetrahydro-2,4-dioxo- (6CI, 7CI, 9CI) (CA INDEX NAME)



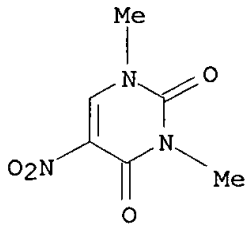
RN 26305-13-5 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 5,6-dimethyl- (9CI) (CA INDEX NAME)



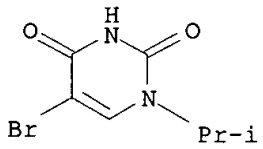
RN 33443-58-2 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 6-methyl-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



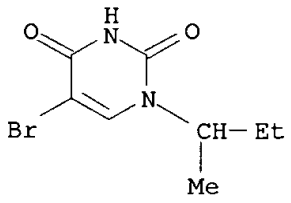
RN 41613-26-7 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1,3-dimethyl-5-nitro- (9CI) (CA INDEX NAME)



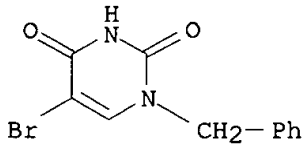
RN 57712-64-8 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 5-bromo-1-(1-methylethyl)- (9CI) (CA INDEX NAME)



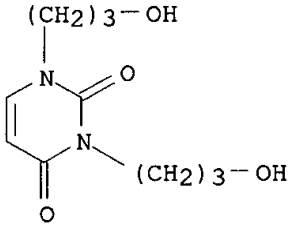
RN 57712-66-0 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 5-bromo-1-(1-methylpropyl)- (9CI) (CA INDEX NAME)



RN 57712-67-1 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 5-bromo-1-(phenylmethyl)- (9CI) (CA INDEX NAME)

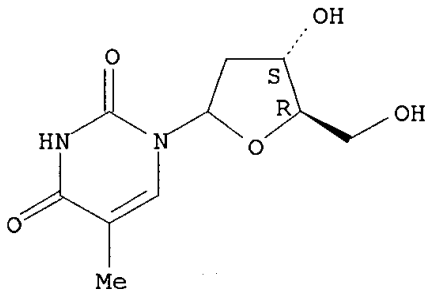


RN 116371-83-6 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1,3-bis(3-hydroxypropyl)- (9CI) (CA INDEX NAME)

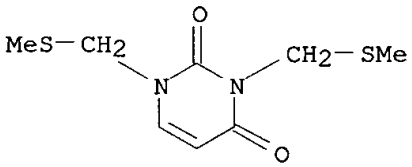


RN 137121-87-0 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-(2-deoxy-D-erythro-pentofuranosyl)-5-methyl- (9CI) (CA INDEX NAME)

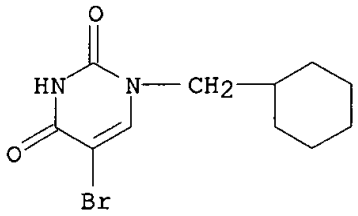
Absolute stereochemistry.



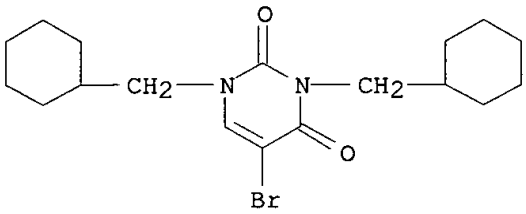
RN 200279-12-5 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1,3-bis[(methylthio)methyl]- (9CI) (CA INDEX NAME)



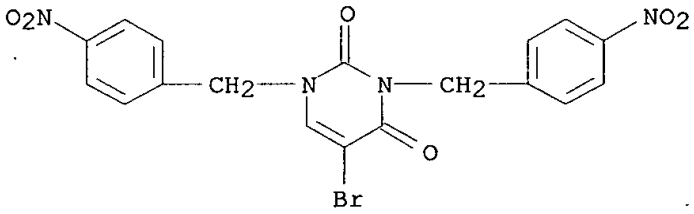
RN 473450-42-9 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 5-bromo-1-(cyclohexylmethyl)- (9CI) (CA INDEX NAME)



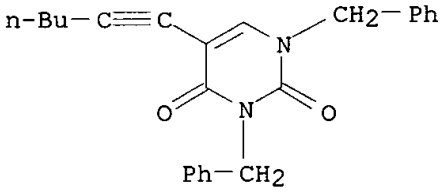
RN 473450-45-2 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 5-bromo-1,3-bis(cyclohexylmethyl)- (9CI) (CA INDEX NAME)



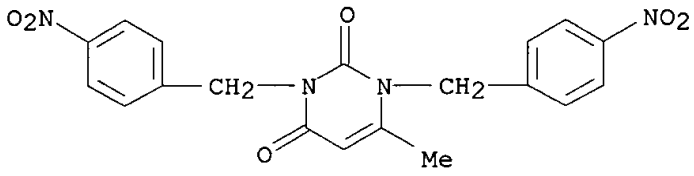
RN 473450-48-5 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 5-bromo-1,3-bis[(4-nitrophenyl)methyl]- (9CI) (CA INDEX NAME)



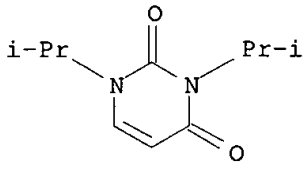
RN 473450-56-5 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 5-(1-hexynyl)-1,3-bis(phenylmethyl)- (9CI) (CA INDEX NAME)



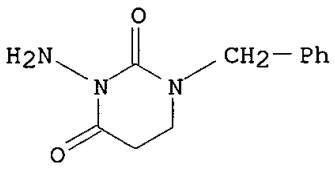
RN 473450-70-3 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 6-methyl-1,3-bis[(4-nitrophenyl)methyl]- (9CI) (CA INDEX NAME)



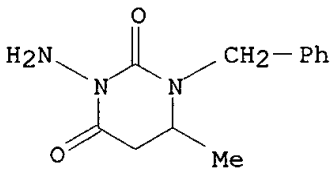
RN 473450-79-2 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1,3-bis(1-methylethyl)- (9CI) (CA INDEX NAME)



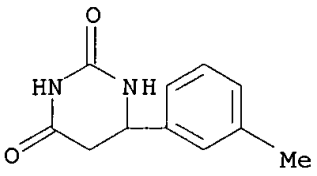
RN 473450-82-7 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 3-aminodihydro-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



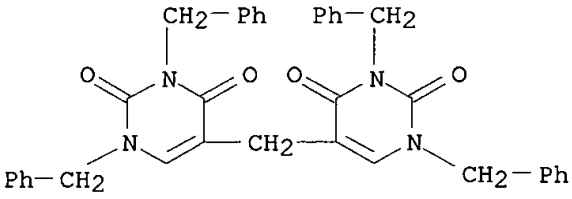
RN 473450-83-8 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 3-aminodihydro-6-methyl-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



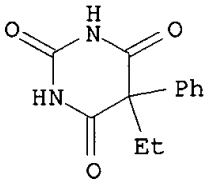
RN 473450-84-9 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, dihydro-6-(3-methylphenyl)- (9CI) (CA INDEX NAME)



RN 473450-86-1 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 5,5'-methylenebis[1,3-bis(phenylmethyl)- (9CI) (CA INDEX NAME)

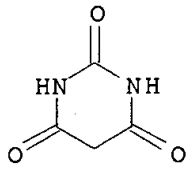


L13 ANSWER 2 OF 23 CAPLUS COPYRIGHT 2003 ACS
AN 2002:512153 CAPLUS
DN 138:163314
TI P-Glycoprotein-mediated efflux of phenobarbital, lamotrigine, and felbamate at the blood-brain barrier: evidence from microdialysis experiments in rats
AU Potschka, Heidrun; Fedrowitz, Maren; Loscher, Wolfgang
CS Department of Pharmacology, Toxicology, and Pharmacy, School of Veterinary Medicine, Hannover, D-30559, Germany
SO Neuroscience Letters (2002), 327(3), 173-176
CODEN: NELED5; ISSN: 0304-3940
PB Elsevier Science Ireland Ltd.
DT Journal
LA English
AB Although a series of new antiepileptic drugs (AEDs) have been launched in the last two decades, drug-refractoriness remains a major problem concerning 20-30% of epileptic patients. The fact that most patients with refractory epilepsy are resistant to several AEDs acting via different targets points to an involvement of unspecific mechanisms like changes in local uptake of AEDs in the epileptic focus region. Increased expression of multidrug transporters has been reported in **epileptogenic** brain tissue from pharmacoresistant patients undergoing epilepsy surgery. However, only limited information exists on the extent to which AEDs are transported by multidrug transporters like P-glycoprotein (PGP). In the present study, the effect of PGP **inhibition** by verapamil on brain access of the AEDs phenobarbital, lamotrigine, and felbamate was investigated by in vivo microdialysis in rats. Local perfusion of verapamil via the microdialysis probe increased the concn. of the three AEDs in the extracellular fluid of the cerebral cortex in a significant manner. The data indicate that overexpression of PGP in epileptic tissue is likely to limit brain access of the AEDs phenobarbital, lamotrigine, and felbamate, thus favoring the hypothesis that multidrug transporters play a crucial role in the phenomenon of drug-refractory epilepsy.
IT **50-06-6**, Phenobarbital, biological studies
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(P-Glycoprotein-mediated efflux of phenobarbital, lamotrigine, and felbamate at the blood-brain barrier with evidence from microdialysis expts. in rats)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)



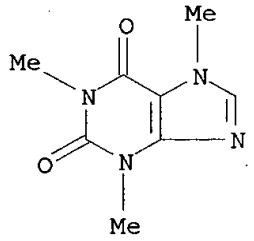
RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 23 CAPLUS COPYRIGHT 2003 ACS
AN 2001:427618 CAPLUS
DN 135:251301
TI The new generation of GABA enhancers: Potential in the treatment of epilepsy
AU Czuczwar, Stanislaw J.; Patsalos, Philip N.
CS Department of Pathophysiology, Medical University, Lublin, Pol.
SO CNS Drugs (2001), 15(5), 339-350
CODEN: CNDREF; ISSN: 1172-7047
PB Adis International Ltd.
DT Journal; General Review
LA English
AB A review with 76 refs. .gamma.-Aminobutyric acid (GABA) is considered to be the major **inhibitory** neuro-transmitter in the brain and loss of GABA **inhibition** has been clearly implicated in **epileptogenesis**. GABA interacts with 3 types of receptor: GABAA, GABAB and GABAC. The GABAA receptor has provided an excellent target for the development of drugs with an anticonvulsant action. Some clin. useful anti-convulsants, such as the benzodiazepines and barbiturates and possibly valproic acid (sodium valproate), act at this receptor. In recent years 4 new anticonvulsants, namely vigabatrin, tiagabine, gabapentin and topiramate, with a mechanism of action considered to be primarily via an effect on GABA, have been licensed. Vigabatrin elevates brain GABA levels by **inhibiting** the enzyme GABA transaminase which is responsible for intracellular GABA catabolism. In contrast, tiagabine elevates synaptic GABA levels by **inhibiting** the GABA uptake transporter, GAT1, and preventing the uptake of GABA into neurons and glia. Gabapentin, a cyclic analog of GABA, acts by enhancing GABA synthesis and also by decreasing neuronal calcium influx via a specific subunit of voltage-dependent calcium channels. Topiramate acts, in part, via an action on a novel site of the GABAA receptor. Although these drugs are useful in some patients, overall, they have proven to be disappointing as they have had little impact on the prognosis of patients with intractable epilepsy. Despite this, addnl. GABA enhancing anticonvulsants are presently under development. Ganaxolone, retigabine and pregabalin may prove to have a more advantageous therapeutic profile than the presently licensed GABA enhancing drugs. This anticipation is based on 2 characteristics. First, they act by hitherto unique mechanisms of action in enhancing GABA-induced neuronal **inhibition**. Secondly, they act on addnl. antiepileptogenic mechanisms. Finally, CGP 36742, a GABAB receptor antagonist, may prove to be particularly useful in the management of primary generalized absence seizures. The exact impact of these new GABA-enhancing drugs in the treatment of epilepsy will have to await their licensing and a period of postmarketing surveillance. As to clarification of their role in the management of epilepsy, this will have to await further clin. trials, particularly direct comparative trials with other anticonvulsants.
IT **67-52-7**, 2,4,6(1H,3H,5H)-Pyrimidinetrione
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(derivs., barbiturates; treatment of epilepsy with new generation of GABA enhancers)
RN 67-52-7 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione (9CI) (CA INDEX NAME)



RE.CNT 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 23 CAPLUS COPYRIGHT 2003 ACS
AN 1999:479180 CAPLUS
DN 131:331964
TI **Epileptogenic** action of caffeine during anoxia in the neonatal rat hippocampus
AU Dzhala, Volodymyr; Desfreres, Luc; Melyan, Zare; Ben-Ari, Yehezkiel; Khazipov, Roustem
CS Division of Regulatory Cell Systems, Institute of Biochemistry of National Academy of Science of Ukraine, Lvov, 290005, Ukraine
SO Annals of Neurology (1999), 46(1), 95-102
CODEN: ANNED3; ISSN: 0364-5134
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB Low concns. of caffeine generated seizure-like effects when applied in conjunction with brief anoxic episodes to the hippocampus of neonatal rats in vitro. In control conditions, brief (4-6-min) anoxic episodes reversibly depressed evoked synaptic responses and blocked the physiol. pattern of network activity. In the presence of caffeine (50 .mu.M), similar anoxic episodes generated ictal (29%) or interictal (33%) epileptiform activities, often followed during reoxygenation by recurrent spontaneous seizure activity that persisted for several hours. These effects are likely mediated by a blockade of adenosine receptors by caffeine because: (1) in control conditions, caffeine antagonized the **inhibitory** effect of the selective A1 receptor agonist N6-cyclopentyladenosine on excitatory synaptic responses, and (2) the **epileptogenic** effects of caffeine were reproduced by the selective A1 receptor antagonists 8-cyclopentyl-1,3-dipropylxanthine and theophylline. The findings suggest that endogenous adenosine, released during anoxia and acting via A1 receptors, prevents seizures in the neonatal hippocampus and that the antagonism of these receptors by caffeine leads to **epileptogenesis**. This study suggests concerns about the safety of caffeine in the fetus and newborn.
IT **58-08-2**, Caffeine, biological studies
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**epileptogenic** action of caffeine during anoxia in the neonatal rat hippocampus)
RN 58-08-2 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)

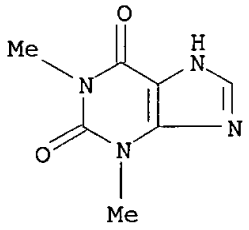


IT **58-55-9**, Theophylline, biological studies **102146-07-6**, 8-Cyclopentyl-1,3-dipropylxanthine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**epileptogenic** action of caffeine response to adenosine

receptor agonists and antagonists during anoxia in the neonatal rat hippocampus)

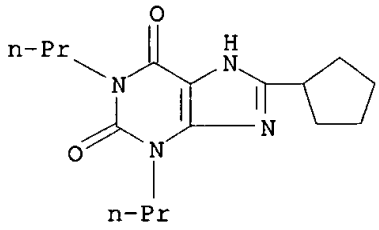
RN 58-55-9 CAPLUS

CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



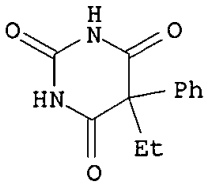
RN 102146-07-6 CAPLUS

CN 1H-Purine-2,6-dione, 8-cyclopentyl-3,7-dihydro-1,3-dipropyl- (9CI) (CA INDEX NAME)



RE.CNT 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

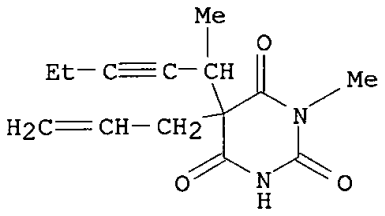
L13 ANSWER 5 OF 23 CAPLUS COPYRIGHT 2003 ACS
AN 1999:256182 CAPLUS
DN 131:43105
TI Brain-derived neurotrophic factor immunoreactivity in the limbic system of rats after acute seizures and during spontaneous convulsions: temporal evolution of changes as compared to neuropeptide Y
AU Vezzani, A.; Ravizza, T.; Moneta, D.; Conti, M.; Borroni, A.; Rizzi, M.; Samanin, R.; Maj, R.
CS Laboratory of Experimental Neurology, Mario Negri Institute for Pharmacological Research, Milan, Italy
SO Neuroscience (Oxford) (1999), 90(4), 1445-1461
CODEN: NRSCDN; ISSN: 0306-4522
PB Elsevier Science Ltd.
DT Journal
LA English
AB Seizures increase the synthesis of brain-derived neurotrophic factor in forebrain areas, suggesting this neurotrophin has biol. actions in epileptic tissue. The understanding of these actions requires information on the sites and extent of brain-derived neurotrophic factor prodn. in areas involved in seizures onset and their spread. In this study, the authors investigated by immunocytochem. the changes in brain-derived neurotrophic factor in the hippocampus, entorhinal and perirhinal cortices of rats at increasing times after acute seizures eventually leading to spontaneous convulsions. The authors also tested the hypothesis that seizure-induced changes in brain-derived neurotrophic factor induce later modifications in neuropeptide Y expression by comparing, in each instance, their immunoreactive patterns. As early as 100 min after seizure induction, brain-derived neurotrophic factor immunoreactivity increased in CA1 pyramidal and granule neurons and in cells of layers II-III of the entorhinal cortex. At later times, immunoreactivity progressively decreased in somata while increasing in fibers in the hippocampus, the subicular complex and in specific layers of the entorhinal and perirhinal cortices. Changes in neuropeptide Y immunoreactivity were superimposed upon and closely followed those of brain-derived neurotrophic factor. One week after seizure induction, brain-derived neurotrophic factor and neuropeptide Y immunoreactivities were similar to controls in 50% of rats. In rats experiencing spontaneous convulsions, brain-derived neurotrophic factor and neuropeptide Y immunoreactivity was strongly enhanced in fibers in the hippocampus/parahippocampal gyrus and in the temporal cortex. In the dentate gyrus, changes in immunoreactivity depended on sprouting of mossy fibers as assessed by growth-assocd. protein-43-immunoreactivity. These modifications were **inhibited** by repeated anticonvulsant treatment with phenobarbital. The dynamic and temporally-linked alterations in brain-derived neurotrophic factor and neuropeptide Y in brain regions critically involved in **epileptogenesis** suggest a functional link between these two substances in the regulation of network excitability.
IT **50-06-6**, Phenobarbital, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(BDNF and neuropeptide Y immunoreactivity in spontaneously epileptic rat in relation to phenobarbital anticonvulsant treatment)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)



RE.CNT 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

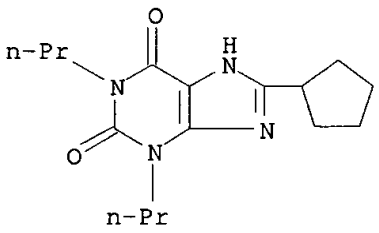
L13 ANSWER 6 OF 23 CAPLUS COPYRIGHT 2003 ACS
AN 1999:157774 CAPLUS
DN 130:333172
TI Extracellular single-unit recordings of piriform cortex neurons in rats: Influence of different types of anesthesia and characterization of neurons by pharmacological manipulation of serotonin receptors
AU Bloms-Funke, Petra; Gernert, Manuela; Ebert, Ulrich; Loscher, Wolfgang
CS Department of Pharmacology, Toxicology, and Pharmacy, School of Veterinary Medicine, Bunteweg, Hannover, Germany
SO Journal of Neuroscience Research (1999), 55(5), 608-619
CODEN: JNREDK; ISSN: 0360-4012
PB Wiley-Liss, Inc.
DT Journal
LA English
AB In epilepsy research, there is a growing interest in the role of the piriform cortex (PC) in the development and maintenance of limbic kindling and other types of limbic **epileptogenesis** leading to complex partial seizures. Neurophysiol. studies on PC or amygdala-PC slice prepns. from kindled rats showed that kindling of the amygdala induces long-lasting changes in synaptic efficacy in the ipsilateral PC, including spontaneous discharges and enhanced susceptibility of PC neurons to evoked burst responses. These long-lasting electrophysiol. changes in the PC during kindling appear to be due, at least in part, to impaired function of GABAergic interneurons. The aim of the present study was to develop an anesthetic protocol allowing electrophysiol. single-unit recordings from **inhibitory**, presumably GABAergic PC interneurons in vivo. In addn. to recording of spontaneously active PC neurons, microiontophoretic application of glutamate was used to activate silent neurons. Anesthesia of rats with ketamine/xylazine was not suited for single-unit recordings in the PC because of marked cardiovascular depression. Anesthesia with chloral hydrate allowed recording of spontaneous or glutamate-driven single-unit activity in .apprx.40% of all animals. A similar percentage was obtained when recordings were done with the narcotic opioid fentanyl (plus gallamine), after all surgical prepns. were performed under anesthesia with repeated administration of the barbiturate methohexital. To avoid brain accumulation of methohexital by repeated applications, we modified the anesthetic protocol in that methohexital was only injected once for initiation of surgical anesthesia, followed by the short-acting anesthetic propofol which does not accumulate upon repeated application. Again, after surgical prepn., electrophysiol. recordings were done under fentanyl (plus gallamine). By this procedure, spontaneous or glutamate-driven single-unit activity could be measured in all rats in either layer II or III of the PC. Based on shape and frequency of action potentials, two types of neurons were recorded. The predominant type was similar in its firing characteristics to GABAergic neurons in other brain regions, was mainly located in layer III, and could be suppressed by the serotonin2A receptor antagonist MDL 100907, suggesting that this type of PC neuron represents **inhibitory**, putative GABAergic interneurons. This new in vivo prepn. may be useful for evaluation of PC neurons in kindled rats.
IT **151-83-7**, Methohexital
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(piriform cortex neuron glutamic acid-driven extracellular single-unit recordings in kindled rats and influence of different types of anesthesia and serotonin receptor characterization therein)
RN 151-83-7 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 1-methyl-5-(1-methyl-2-pentynyl)-5-(2-

propenyl)- (9CI) (CA INDEX NAME)



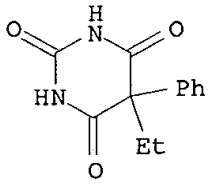
RE.CNT 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 7 OF 23 CAPLUS COPYRIGHT 2003 ACS
AN 1998:553892 CAPLUS
DN 129:340084
TI A comparison of the adenosine-mediated synaptic **inhibition** in the CA3 area of immature and adult rat hippocampus
AU Descombes, Severine; Avoli, Massimo; Psarropoulou, Caterina
CS Faculty of Medicine, Department of Physiology and Biophysics, University of Sherbrooke, Sherbrooke, QC, J1H 5N4, Can.
SO Developmental Brain Research (1998), 110(1), 51-59
CODEN: DBRRDB; ISSN: 0165-3806
PB Elsevier Science B.V.
DT Journal
LA English
AB The authors compared the effects of the adenosine A1 receptor activation on the postsynaptic potentials (psps) recorded from the CA3 area of immature (postnatal days 10-20) and adult rat hippocampal neurons in vitro. The adenosine A1 receptor agonist 2-phenyl-isopropyl-adenosine (PIA, 1 .mu.M) depressed the stimulus-induced psps less in immature and more in adult neurons. In the presence of the GABAA receptor antagonist bicuculline methiodide (BMI, 10 .mu.M), PIA reduced the duration and no. of action potentials of the stimulus-induced paroxysmal depolarizations (PDs) in immature neurons, while it blocked PDs in adult neurons. Spontaneous BMI-induced PDs, were blocked by PIA in less than half (5/12) immature and all (6/6) adult neurons. The adenosine A1 receptor antagonist 8-cyclopentyl-1,3-dipropylxanthine (DPCPX, 1 .mu.M) enhanced the stimulus-induced psps in immature and adult neurons alike; this effect did not lead to stimulus-induced bursting in immature neurons. DPCPX induced spontaneous bursts (proconvulsant effect) in only 2/16 immature but in all adult (12/12) neurons. In BMI, DPCPX increased the duration and no. of action potentials of the stimulus-induced PDs in immature and adult neurons alike (by about 30%), but it increased the rates of occurrence of spontaneous PDs in significantly more adult neurons. In conclusion, the authors' results suggest that adenosine, acting via A1 receptors, is a more effective endogenous anti-epileptic in adult than in immature hippocampus, a fact which may contribute to the susceptibility of the latter to **epileptogenesis**.
IT **102146-07-6**, 8-Cyclopentyl-1,3-dipropylxanthine
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(comparison of the adenosine-mediated synaptic **inhibition** in the CA3 area of immature and adult rat hippocampus)
RN 102146-07-6 CAPLUS
CN 1H-Purine-2,6-dione, 8-cyclopentyl-3,7-dihydro-1,3-dipropyl- (9CI) (CA INDEX NAME)

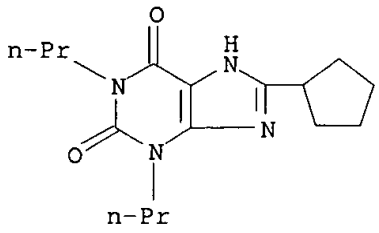


RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD

L13 ANSWER 8 OF 23 CAPLUS COPYRIGHT 2003 ACS
AN 1997:16851 CAPLUS
DN 126:102499
TI The contribution of endogenous mono-ADP-ribosylation to kindling-induced **epileptogenesis**
AU Suzuki, Kaori; Iwasa, Hiroto; Kikuchi, Shuichi; Sato, Toshio; Miyake, Masami; Morinaga, Naoko; Noda, Masatoshi
CS Department of Neuropsychiatry, Chiba University School of Medicine, 1-8-1 Inohana, Chuo-ku, Chiba, 260, Japan
SO Brain Research (1997), 745(1,2), 109-113
CODEN: BRREAP; ISSN: 0006-8993
PB Elsevier
DT Journal
LA English
AB The authors examd. the alteration of endogenous mono ADP-ribosylation in the hippocampus of amygdaloid kindled rats to clarify the neurochem. basis of epilepsy. A significant increase of the ADP-ribosylation on the 38 kDa protein was obsd. in the hippocampal membrane of the kindled rat. Several antiepileptics (phenytoin, phenobarbital, carbamazepine, sodium valproate) significantly decreased the ADP-ribosylation on the 38 kDa protein and effaced the increase in the kindled group. The ADP-ribosylation was largely increased by sodium nitroprusside, a nitric oxide generating compd., in both the kindled and control groups. Carbamazepine could not affect the ADP-ribosylation in the presence of sodium nitroprusside. Twenty amino acids from the N-terminus of the ADP-ribosylated 38 kDa protein were detd. by sequential anal. The sequence was completely identical to that of glyceraldehyde-3-phosphate dehydrogenase. These results indicate that the endogenous mono-ADP-ribosylation which increased in the kindled group and decreased by the antiepileptics might be a specific reaction assocd. with the mechanisms of **epileptogenesis**.
IT **50-06-6**, Phenobarbital, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hippocampal endogenous mono-ADP-ribosylation of glyceraldehyde-3-phosphate dehydrogenase-related 38-kDa protein response to kindling-induced **epileptogenesis** and **inhibition** by antiepileptics)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)



L13 ANSWER 9 OF 23 CAPLUS COPYRIGHT 2003 ACS
AN 1995:922795 CAPLUS
DN 124:45424
TI Opposite modulation of 4-aminopyridine and hypoxic hyperexcitability by A1 and A2 adenosine receptor ligands in rat hippocampal slices
AU Longo, R.; Zeng, Y. C.; Sagratella, S.
CS Laboratorio di Farmacologia, Istituto Superiore Di Sanita, Viale Regina Elena 299, Rome, 00161, Italy
SO Neuroscience Letters (1995), 200(1), 21-4
CODEN: NELED5; ISSN: 0304-3940
PB Elsevier
DT Journal
LA English
AB The effects of the adenosine receptor antagonist 1,3-dipropyl-8-cyclopentylxanthine (DPCPX), and of the adenosine agonists N6-cyclopentyladenosine (CPA), N6-(2-phenylisopropyl)adenosine (R-PIA), and 2-[p-(carboxyethyl)phenylethylamino]-5'-N-ethylcarboxamidoadenosine (CGS 21680) were investigated on the hyperexcitability induced in the CA1 area of rat hippocampal slices by hypoxia or the **epileptogenic** agent 4-aminopyridine. Slice perfusion with the mixed adenosine receptor agonist R-PIA (0.2 .mu.M) significantly decreased: (i) the no. of slices showing a transient CA1 epileptiform bursting during the hypoxic period; (ii) the duration of the hypoxia-induced epileptiform bursting. Conversely, slice perfusion with the selective A1 adenosine receptor antagonists DPCPX (0.2 .mu.M) or with the selective A2 adenosine receptor agonist CGS 21680 significantly increased the no. of slices showing a transient CA1 epileptiform bursting during the hypoxic period but did not affect the duration of the hypoxia-induced epileptiform bursting. Neither drug significantly affected the no. of slices showing functional recovery after hypoxia. Slice perfusion with DPCPX (0.2 .mu.M) also significantly increased the no. of slices showing a persistent CA1 epileptiform bursting during the reoxygenation period, while the other drugs failed to affect it. Slice perfusion with the selective A1 adenosine receptor agonist CPA (2 .mu.M) or R-PIA (5 .mu.M) significantly decreased the duration of the CA1 epileptiform bursting induced by 100 .mu.M 4-aminopyridine. CGS 21680 (5 .mu.M) perfused together with CPA (2 .mu.M) significantly counteracted the **inhibitory** effects of the A1 adenosine receptor agonist on 4-aminopyridine epileptiform bursting, while it failed by itself to directly affect the 4-aminopyridine epileptiform bursting duration. The results produce evidence for a selective opposite modulation by A1 and A2 adenosine agonists in the control of hippocampal hyperexcitability induced by hypoxia or 4-aminopyridine but not in the post-hypoxic functional recovery.
IT **102146-07-6**, 1,3-Dipropyl-8-cyclopentylxanthine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(opposite modulation of 4-aminopyridine and hypoxic hyperexcitability by A1 and A2 adenosine receptor ligands in rat hippocampal slices)
RN 102146-07-6 CAPLUS
CN 1H-Purine-2,6-dione, 8-cyclopentyl-3,7-dihydro-1,3-dipropyl- (9CI) (CA INDEX NAME)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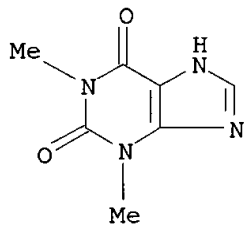
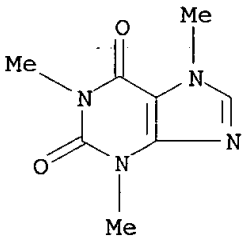
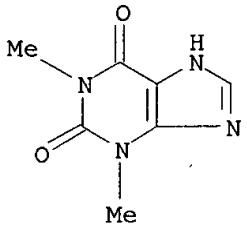
L13 ANSWER 10 OF 23 CAPLUS COPYRIGHT 2003 ACS
AN 1995:210981 CAPLUS
DN 123:694
TI The effects of the purinergic system on digitalis-induced epileptiform activity
AU Kesim, Yuksel; Marangoz, Cafer; Ayyildiz, Mustafa; Tasci, Niyazi; Agar, Erdal; Sahinoglu, Haydar
CS Faculty Medicine, University Ondokuz Mayis, Samsun, Turk.
SO Journal of Basic and Clinical Physiology and Pharmacology (1994), 5(2), 167-78
CODEN: JBPPES; ISSN: 0334-1534
DT Journal
LA English
AB It has been suggested that endogenous chem. substances, such as adenosine, released during a seizure attack, may act as anticonvulsants in vivo. The authors have investigated electrophysiol. the effects of purinoceptor agonists and antagonists on the epileptiform activity induced by intracortical digitalis in anesthetized rats. Intracortical injections of 1, 2, or 4 .mu.g digitalis (desacetyl lanatocid C) caused an epileptiform electrocorticogram (ECoG). The application of adenosine (25 or 100 .mu.M) or ATP (3 mM) after desacetyl lanatocid C blocked the epileptiform activity. .beta.,.gamma.-Methylene ATP (0.1-0.8 mM), a stable analog of ATP, produced **inhibition** and then death. The **epileptogenic** effect of desacetyl lanatocid C was enhanced by theophylline (1 mM); however, suramin (1 mM) changed the pattern of epilepsy. These results indicate that the purinergic system may be involved in the mechanism of action of digitalis glycosides.
IT **58-55-9**, Theophylline, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(effects of purinergic agents on digitalis-induced epileptiform activity)
RN 58-55-9 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



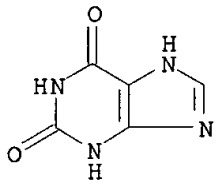
L13 ANSWER 11 OF 23 CAPLUS COPYRIGHT 2003 ACS
AN 1994:235985 CAPLUS
DN 120:235985
TI **Epileptogenic** actions of xanthines in relation to their affinities for adenosine A1 receptors in CA3 neurons of hippocampal slices (guinea pig)
AU Moraidis, Isaak; Bingmann, Dieter
CS Institut fuer Physiologie, IG1, Hufelandstra.beta.e 55, Essen, D-45122, Germany
SO Brain Research (1994), 640(1-2), 140-5
CODEN: BRREAP; ISSN: 0006-8993
DT Journal
LA English
AB To analyze the **epileptogenic** mechanisms of caffeine and related xanthines, putative effects of these drugs were studied on adenosine receptors of CA3 neurons in hippocampal slices. **Epileptogenic** concns. of different xanthine derivs. strongly correlated with their affinities for the **inhibitory** A1 adenosine receptor subtype. The A1 receptor agonists adenosine and R-PIA reversibly depressed xanthine-induced epileptic activity without effects on the resting membrane potential or on spontaneously occurring action potentials. These findings suggest that the **epileptogenic** potency of xanthines is primarily due to the blockade of the A1 receptors through an abnormal rise of intracellular cAMP and to the excessive transmembrane calcium fluxes underlying paroxysmal depolarization shifts.
IT **58-08-2**, Caffeine, biological studies **58-55-9**, Theophylline, biological studies **69-89-6D**, Xanthine, derivs. **83-67-0**, Theobromine **479-18-5**, Diphylline **961-45-5**, 8-Phenyltheophylline **28822-58-4**, 3-Isobutyl-1-methylxanthine **102146-07-6**, 8-Cyclopentyl-1,3-dipropylxanthine
RL: BIOL (Biological study)
(epilepsy from, mechanism of, A1 adenosine receptors blockade in)
RN 58-08-2 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)



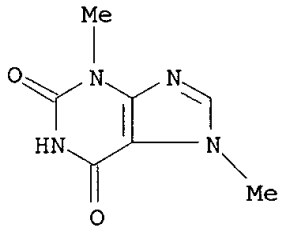
RN 58-55-9 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



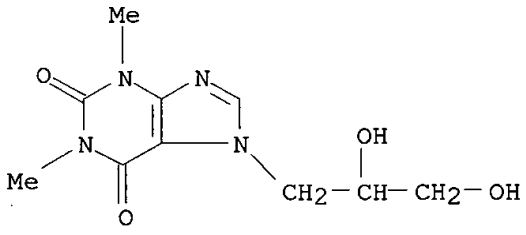
RN 69-89-6 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro- (9CI) (CA INDEX NAME)



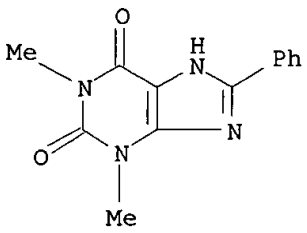
RN 83-67-0 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-3,7-dimethyl- (9CI) (CA INDEX NAME)



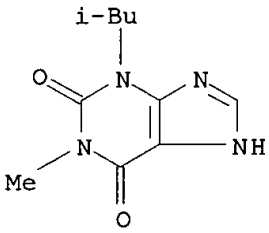
RN 479-18-5 CAPLUS
CN 1H-Purine-2,6-dione, 7-(2,3-dihydroxypropyl)-3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



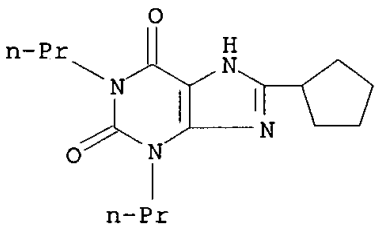
RN 961-45-5 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-8-phenyl- (9CI) (CA INDEX NAME)



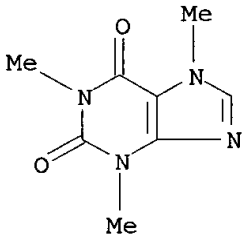
RN 28822-58-4 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1-methyl-3-(2-methylpropyl)- (9CI) (CA INDEX NAME)



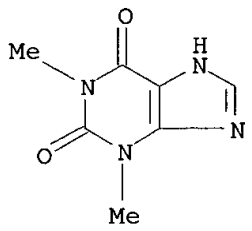
RN 102146-07-6 CAPLUS
CN 1H-Purine-2,6-dione, 8-cyclopentyl-3,7-dihydro-1,3-dipropyl- (9CI) (CA INDEX NAME)



L13 ANSWER 12 OF 23 CAPLUS COPYRIGHT 2003 ACS
AN 1993:623314 CAPLUS
DN 119:223314
TI GABA-responses of CA3 neurons at **epileptogenic** threshold concentrations of convulsants
AU Bonnet, U.; Bingmann, D.
CS Inst. Physiol., Univ. Essen, Essen, 4300/1, Germany
SO NeuroReport (1993), 4(6), 715-18
CODEN: NERPEZ; ISSN: 0959-4965
DT Journal
LA English
AB **Epileptogenic** actions of convulsants are often attributed to weakened **inhibitory** synaptic mechanisms. This assumption was tested by studying GABA-induced postsynaptic membrane potential (MP) changes of CA3 neurons (guinea-pig) before and during exposure to bicuculline methiodide (BMI), pentylenetetrazol (PTZ), penicillin (PEN) and caffeine (CAF). Under control conditions GABA release elicited polyphasic MP fluctuations (components I-III). After adding BMI, PTZ, PEN or CAF, early hyperpolarizations (component I) did not change at **epileptogenic** threshold concns. These convulsants however, exerted differential effects on the depolarizing component II, but only threshold concns. of penicillin strongly reduced the amplitude of this component. Simultaneously, component III was slightly accentuated. These findings indicate that changes of GABA responses are not an essential prerequisite for the generation of paroxysmal depolarizations.
IT **58-08-2**, Caffeine, biological studies
RL: BIOL (Biological study)
(GABA postsynaptic neurotransmission response to **epileptogenic** threshold concns. of, in hippocampus CA3 neurons)
RN 58-08-2 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)



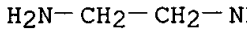
L13 ANSWER 13 OF 23 CAPLUS COPYRIGHT 2003 ACS
AN 1989:289 CAPLUS
DN 110:289
TI Quinolones, theophylline, and diclofenac interactions with the .gamma.-aminobutyric acid receptor
AU Segev, S.; Rehavi, M.; Rubinstein, E.
CS Infect. Dis. Unit, Sheba Med. Cent., Tel-Hashomer, Israel
SO Antimicrobial Agents and Chemotherapy (1988), 32(11), 1624-6
CODEN: AMACCQ; ISSN: 0066-4804
DT Journal
LA English
AB Epileptic seizures and hallucinations, which are rare in patients receiving quinolones, have been obsd. more frequently in patients receiving both quinolones and either theophylline or nonsteroidal anti-inflammatory drugs. **Inhibition** of GABA binding to the GABA receptor, resulting in general excitation of the central nervous system, may be the underlying mechanism of these adverse phenomena. It is demonstrated here that ciprofloxacin displaced a GABA-like substance (muscimol) from the GABA receptor when administered in concns. of >10-4 M. These concns. were lower than those needed by pefloxacin, ofloxacin, and nalidixic acid to reach a concn. that **inhibits** 50% of binding. The combination of ciprofloxacin and theophylline was additive in reducing the level of muscimol binding to the GABA receptor, whereas a diclofenac-ciprofloxacin combination had no effect. The concns. of both ciprofloxacin and the other quinolones used were much higher than those obsd. in human serum and cerebrospinal fluid in a clin. setting; however, different human GABA receptor affinities, preexisting GABA excitation, or underlying central nervous system disease may amplify the excitatory side effects obsd. by the coadministration of quinolones and theophylline. Attention should be paid to the possible **epileptogenic** activity of the simultaneous administration of quinolones with aminophylline, nonsteroidal anti-inflammatory drugs, or other unpredictable drugs.
IT **58-55-9**, Theophylline, biological studies **317-34-0**, Aminophylline
RL: BIOL (Biological study)
(interaction of ciprofloxacin and, with GABAergic receptor)
RN 58-55-9 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



RN 317-34-0 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-, compd. with 1,2-ethanediamine (2:1) (9CI) (CA INDEX NAME)

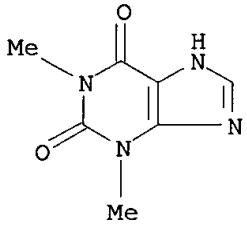
CM 1

CRN 107-15-3
CMF C2 H8 N2

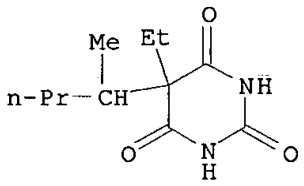


CM 2

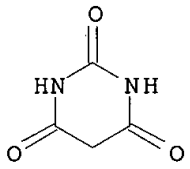
CRN 58-55-9
CMF C7 H8 N4 O2



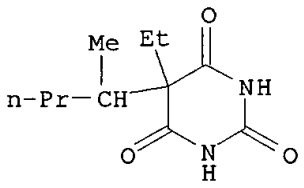
L13 ANSWER 14 OF 23 CAPLUS COPYRIGHT 2003 ACS
AN 1987:591578 CAPLUS
DN 107:191578
TI .gamma.-Hydroxybutyric acid binding sites: evidence for coupling to a chloride anion channel
AU Snead, O. C., III; Nichols, A. C.
CS Sch. Med., Univ. Alabama, Birmingham, AL, USA
SO Neuropharmacology (1987), 26(10), 1519-23
CODEN: NEPHBW; ISSN: 0028-3908
DT Journal
LA English
AB The effect of 8 anions, including Cl-, on the binding of .gamma.-hydroxy [2,3-3H2]butyric acid (GHB) to synaptosomal membranes of rat and human brain was ascertained, as was the effect of a no. of other allosteric modulators of the GABA/benzodiazepine/picrotoxin complex. All ions which were active at the Cl- channel **inhibited** the binding of [3H]GHB in a dose-dependent manner, with max. **inhibition** of binding being 60% at 300 mM of anion. Inactive ions in this binding system included sulfate, acetate, and fluoride, all impermeable to the Cl- channel. The **inhibition** of binding was temp.-dependent, being abolished at 37.degree., and was independent of the cation used. The binding of [3H]GHB was also enhanced by pentobarbital, picrotoxin, and diazepam but unchanged in the presence of GABA, muscimol, bicuculline, baclofen, or strychnine. These data raise the possibility that the **epileptogenic** effect of GHB may be modulated by an action on the Cl- channel that is tightly coupled to the GABA/benzodiazepine/picrotoxin and(or) GHB receptor complex.
IT **76-74-4**, Pentobarbital
RL: BIOL (Biological study)
(hydroxybutyrate binding by brain of human and lab. animal stimulation by)
RN 76-74-4 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-(1-methylbutyl)- (9CI) (CA INDEX NAME)



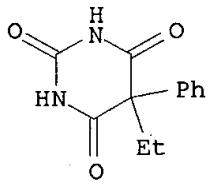
L13 ANSWER 15 OF 23 CAPLUS COPYRIGHT 2003 ACS
AN 1987:573667 CAPLUS
DN 107:173667
TI 4-Aminopyridine **inhibits** synaptosomal plasma membrane protein phosphorylation in vitro: effect of the selective NMDA-antagonist 2-amino-5-phosphonovalerate
AU Heemskerk, F. M. J.; Schrama, L. H.; De Graan, P. N. E.; Gispen, W. H.
CS Rudolf Magnus Inst. Pharmacol., Univ. Utrecht, Utrecht, 3584 CH, Neth.
SO Biochemical and Biophysical Research Communications (1987), 147(1), 94-9
CODEN: BBRCA9; ISSN: 0006-291X
DT Journal
LA English
AB Phosphorylation of synaptosomal plasma membranes (SPM) from rat hippocampus in the presence of the convulsant drug 4-aminopyridine resulted in the **inhibition** of the phosphorylation of the nervous tissue specific protein kinase C substrate protein B-50 [48 kilodaltons (kDa)] and the .alpha.-subunit of calcium/-calmodulin-dependent protein kinase II (50 kDa). Preincubation of SPM with 2-amino-5-phosphonovalerate prevents the **inhibition** of B-50 phosphorylation by 4-aminopyridine, but had no effect on the **inhibition** of 50 kDa phosphorylation. 2-Amino-5-phosphonovalerate is known to be a specific N-methyl-D-aspartate antagonist and has anti-epileptic activity in vitro and in vivo. Several other anti-epileptic drugs tested did not influence the 4-aminopyridine-induced **inhibition** of protein phosphorylation.
IT **67-52-7**, Barbituric acid **76-74-4**, Pentobarbital
RL: BIOL (Biological study)
(aminopyridine convulsant **inhibition** of synaptosomal membrane protein phosphorylation response to)
RN 67-52-7 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione (9CI) (CA INDEX NAME)



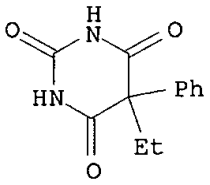
RN 76-74-4 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-(1-methylbutyl)- (9CI) (CA INDEX NAME)



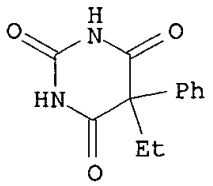
L13 ANSWER 16 OF 23 CAPLUS COPYRIGHT 2003 ACS
AN 1984:432887 CAPLUS
DN 101:32887
TI **Epileptogenic** effect of cephalosporins. II. **Epileptogenic** effect of certain cephalosporins administered intravenously to rats and antiepileptic effect of certain anticonvulsants in cefazolin-induced seizure
AU Ikegami, Nobuyuki
CS Dent. Sch., Okayama Univ., Okayama, 700, Japan
SO Okayama Igakkai Zasshi (1983), 95(11/12), 1363-81
CODEN: OIZAAV; ISSN: 0030-1558
DT Journal
LA Japanese
AB Ceftezole [26973-24-0], cefotiam [61622-34-2], cefazolin [25953-19-9], cephaloridine [50-59-9], cefapirin [21593-23-7], and cefmetazole [56796-20-4], injected intraventricularly, had an **epileptogenic** action in rats, and the i.v. injection of the 1st 4 of these drugs (200-1000 mg/kg) caused a similar effect. The epilepsy was suppressed by i.v. injection of diazepam [439-14-5] or phenobarbital [**50-06-6**]. Phenytoin [57-41-0] was effective only against cephaloridine.
IT **50-06-6**, biological studies
RL: BIOL (Biological study)
(epilepsy from cephalosporins **inhibition** by)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)



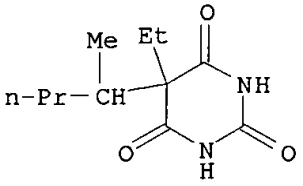
L13 ANSWER 17 OF 23 CAPLUS COPYRIGHT 2003 ACS
AN 1983:400410 CAPLUS
DN 99:410
TI Hypermethylation in the MSO-**epileptogenic** brain: reversal by dilantin or phenobarbital
AU Schatz, Robert A.; Wilens, Timothy E.; Tatter, Stephen B.; Sellinger, Otto Z.
CS Toxicol. Program, Northeast. Univ., Boston, MA, 02115, USA
SO Biochem. S-Adenosylmethionine Relat. Compd., Proc. Conf. (1982), Meeting Date 1981, 675-8 Publisher: Macmillan, London, UK.
CODEN: 49REAA
DT Conference
LA English
AB In mice, chronic phenobarbital (I) [**50-06-6**] decreased the brain S-adenosyl-L-methionine (AdoMet) [29908-03-0] and did not prevent the L-methionine-d,l-sulfoximine (MSO) [15985-39-4]-induced decreased in AdoMet whereas dilantin (II) [630-93-3] had no effect on brain AdoMet levels, but prevented the decrease in AdoMet caused by MSO treatment. Both I and II induced large increases in the brain levels of the AdoMet demethylation product S-adenosyl-L-homocysteine (AdoHyc) [979-92-0]. In mice treated with MSO and either anticonvulsant, AdoHyc levels were near those of the controls. Brain protein carboxymethylation was decreased by I but not by II; prior treatment with either I or II, however, prevented the MSO-induced increase in protein carboxymethylation. I and II were equally effective in their ability to increase MSO seizure latency and abolish the tonic component of MSO seizures. Thus, I and II are capable of slowing transmethylation reactions and reverse, in part, MSO-induced hypermethylation and also to decrease the incidence and severity of MSO-induced seizures, indicating that a cause-effect relationship may exist between increased protein carboxymethylation (or other methylation reactions) and MSO seizures.
IT **50-06-6**, biological studies
RL: BIOL (Biological study)
(convulsion and methylation by brain induction by methionine sulfoxamine response to)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)



L13 ANSWER 18 OF 23 CAPLUS COPYRIGHT 2003 ACS
AN 1983:101044 CAPLUS
DN 98:101044
TI The effects of convulsant and anticonvulsant drugs on the release of radiolabeled GABA, glutamate, noradrenaline, serotonin and acetylcholine from rat cortical slices
AU De Boer, T.; Stoof, J. C.; Van Duijn, H.
CS Med. Fac., Free Univ., Amsterdam, 1007 MC, Neth.
SO Brain Research (1982), 253(1-2), 153-60
CODEN: BRREAP; ISSN: 0006-8993
DT Journal
LA English
AB A possible presynaptic site of action of convulsant and anticonvulsant drugs was evaluated by studying their effect on depolarization-induced transmitter release using radiolabeled GABA [56-12-2], glutamate [56-86-0], noradrenaline [51-41-2], serotonin [50-67-9], and acetylcholine [51-84-3]. The antiepileptic diphenylhydantoin (I) [57-41-0] **inhibited** the release of noradrenaline and serotonin at concns. that had antiepileptic activity in vivo. The release of the other transmitters was affected only with higher concns. phenobarbital (PhB) [**50-06-6**] reduced the release of all transmitters studied at concns. much above the levels that are considered antiepileptic in vivo. Comparison with the anesthetic barbiturate pentobarbital [**76-74-4**] further indicated that the presynaptic effects of PhB were related to its sedative rather than antiepileptic properties. diazepam [439-14-5] And valproate [99-66-1] had little effect; only GABA release was slightly reduced with diazepam at the highest concn. studied. The convulsants penicillin [61-33-6] and pentylenetetrazole [54-95-5] both increased the release of glutamate at concns. that induce epileptiform activity in vivo or in vitro. Other transmitter systems were differentially affected by the 2 convulsants. A small increase of noradrenaline and serotonin release was obsd. with penicillin, but not with pentylenetetrazole. A presynaptic site of action for some, but not all, **epileptogenic** and antiepileptic drugs probably exists in addn. to other, postsynaptic mechanisms. Glutamate is probably a major excitatory neurotransmitter in the brain and many physiol. studies have suggested a role of excitatory pathways in the generation of epileptiform activity.
IT **50-06-6**, biological studies **76-74-4**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(neurotransmitter release by brain response to)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)



RN 76-74-4 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-(1-methylbutyl)- (9CI) (CA INDEX NAME)


Me
Et
O
n-Pr—CH
NH
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N
H
O

L13 ANSWER 19 OF 23 CAPLUS COPYRIGHT 2003 ACS
AN 1979:750 CAPLUS
DN 90:750
TI Uptake and release of norepinephrine by slices of rat cerebral cortex: Effect of agents that increase cyclic AMP levels
AU Walker, Jonathan E.; Goodman, Patsy; Jacobs, Donald; Lewin, Edward
CS Neurol. Serv., VA Hosp., Dallas, TX, USA
SO Neurology (1978), 28(9, Pt. 1), 900-4
CODEN: NEURAI; ISSN: 0028-3878
DT Journal
LA English
AB Cerebral cortical slices from rats were incubated in physiol. saline, and the uptake, release, and K+-stimulated release of norepinephrine (I) [51-41-2] were measured. Dibutyryl cyclic AMP [362-74-3], the phosphodiesterase **inhibitors** aminophylline [**317-34-0**] and papaverine [58-74-2], and adenosine [58-61-7] (which stimulates adenyl cyclase) all caused a variable increase in uptake of I at concns. ranging from 10-7 to 10-4 M. PGE1 [745-65-3] and PGE2 [363-24-6] appeared to have no effect on uptake, but this may be because the alc. required to dissolve them had an **inhibitory** effect on uptake. None of these compds. appeared to affect basal or K+-stimulated release of I. These agents therefore seem to have an effect opposite to that of the tricyclic antidepressants (which **inhibit** uptake of I). Since I postsynaptic effects are usually **inhibitory** in the cortex, the stimulatory effect of the drugs tested on the presynaptic uptake of I may explain the stimulant and **epileptogenic** effects of these drugs.
IT **317-34-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(norepinephrine metab. by brain response to)
RN 317-34-0 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-, compd. with 1,2-ethanediamine (2:1) (9CI) (CA INDEX NAME)

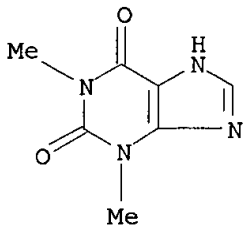
CM 1

CRN 107-15-3
CMF C2 H8 N2

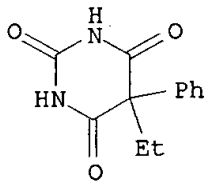
$H_2N-CH_2-CH_2-NH_2$

CM 2

CRN 58-55-9
CMF C7 H8 N4 O2


O
Me
H
N
N
N
O
N
Me

L13 ANSWER 20 OF 23 CAPLUS COPYRIGHT 2003 ACS
AN 1977:11778 CAPLUS
DN 86:11778
TI Action of antiepileptic drugs on cortical induced **epileptogenic** activity
AU Gardner, C. R.; Gartside, I. B.; Webster, R. A.
CS Dep. Pharmacol., Univ. Coll. London, London, UK
SO Epilepsy, Proc. Hans Berger Centen. Symp. (1974), Meeting Date 1973, 105-10. Editor(s): Harris, Phillip; Mawdsley, Clifford. Publisher: Churchill-Livingstone, London, Engl.
CODEN: 34ARAK
DT Conference
LA English
AB Trimethadione [127-48-0] (60-120 mg/kg, i.v.) reversed the leptazol-induced changes in the direct cortical response to elec. stimulation of the cortex. Larger doses (120-200 mg/kg, i.v.) were required to reverse bicuculline-induced changes. When the leptazol effect was severe, trimethadione decreased the rebound wave, leaving the initial wave and the **inhibitory** wave relatively unaffected. This suggests that trimethadione preferentially decreases transmission in the neurons of the corticothalamocortical pathway which mediates the rebound wave. Large i.v. or i.p. doses of phenobarbitone [**50-06-6**] (30-60 mg/kg) were equally effective in decreasing both leptazol or bicuculine-induced changes in the direct corticol response. However, it rarely completely reversed convulsant effects without depressing corticol cell firing below preconvulsant levels. Phenytoin [630-93-3] (20-30 mg/kg, i.v.) had no depressant effect on the normal or convulsant-modified direct vertical response. It is suggested that the direct cortical response in the presence of subconvulsive doses of convulsant drugs may be a useful system with which to study the genesis and spread of **epileptogenic** activity.
IT **50-06-6**, biological studies
RL: BIOL (Biological study)
(brain elec. activity response to, epilepsy in relation to)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)



L13 ANSWER 21 OF 23 CAPLUS COPYRIGHT 2003 ACS
AN 1976:538053 CAPLUS
DN 85:138053
TI Production of epileptiform discharges by application of agents which increase cyclic AMP levels in rat cortex
AU Walker, J. E.; Lewin, E.; Moffitt, B. C.
CS Sect. Neurol., VA Hosp., Denver, CO, USA
SO Epilepsy, Proc. Hans Berger Centen. Symp. (1974), Meeting Date 1973, 30-6. Editor(s): Harris, Phillip; Mawdsley, Clifford. Publisher: Churchill-Livingstone, London, Engl.
CODEN: 34ARAK
DT Conference
LA English
AB In rats, agents which increase cyclic AMP [60-92-4] by diffusion (dibutyryl cyclic AMP [362-74-3]), stimulation of adenylate cyclase (adenosine [58-61-7]) or **inhibition** of phosphodiesterase (aminophylline [**317-34-0**]) produced epileptiform activity when applied to the cerebral cortex.
IT **317-34-0**
RL: BIOL (Biological study)
(epilepsy from, cyclic AMP in relation to)
RN 317-34-0 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-, compd. with 1,2-ethanediamine (2:1) (9CI) (CA INDEX NAME)

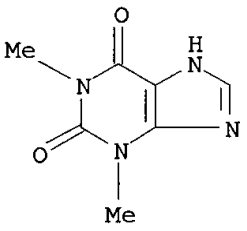
CM 1

CRN 107-15-3
CMF C2 H8 N2

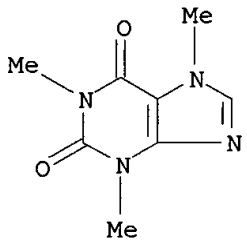
$H_2N-CH_2-CH_2-NH_2$

CM 2

CRN 58-55-9
CMF C7 H8 N4 O2



IT **58-08-2**, biological studies
RL: PRP (Properties)
(epilepsy from, cyclic AMP in relation to)
RN 58-08-2 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)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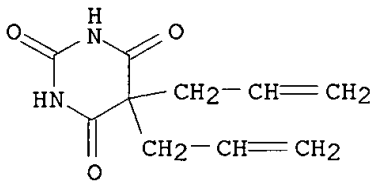
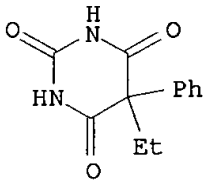
L13 ANSWER 22 OF 23 CAPLUS COPYRIGHT 2003 ACS
AN 1974:128209 CAPLUS
DN 80:128209
TI Effects of some antiepileptic and other drugs on the EEG [electroencephalogram] in rats with a cobalt **epileptogenic** focus
AU Chocholova, L.; Radil-Weiss, T.
CS Inst. Physiol., Czech. Acad. Sci., Prague, Czech.
SO Activitas Nervosa Superior (1973), 15(3), 170-1
CODEN: ACNSAX; ISSN: 0001-7604
DT Journal
LA English
AB Allobarbitol [**52-43-7**] (15-50 mg/kg) significantly increased, diphenylhydantoin [630-93-3] (40 mg/kg) did not affect, and diazepam [439-14-5] and chlordiazepoxide [58-25-3] decreased the no. of single spikes in the electroencephalogram of rats with a cobalt epiletogenic focus and lengthened the telencephalic sleep phase. Seizures were completely **inhibited** by barbiturates and benzodiazepines but were increased by diphenylhydantoin, esp. during the first hr. Thus, the anticonvulsants have different modes of action.
IT **52-43-7**
RL: BIOL (Biological study)
(brain elec. activity response to, anticonvulsive activity in relation to)
RN 52-43-7 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5,5-di-2-propenyl- (9CI) (CA INDEX NAME)



L13 ANSWER 23 OF 23 CAPLUS COPYRIGHT 2003 ACS
AN 1969:104983 CAPLUS
DN 70:104983
TI Electroencephalographic and behavioral changes following penicillin injection into the thalamus and its modification by drugs
AU Inutsuka, Tatsumi
CS Univ. Kyushu, Fukuoka, Japan
SO Fukuoka Igaku Zasshi (1969), 60(1), 16-33
CODEN: FKIZA4; ISSN: 0016-254X
DT Journal
LA Japanese
AB Six pairs of bipolar electrodes were chromically implanted into the thalamus, hippocampus, amygdaloid nucleus, caudate nucleus, and frontal and parietal cortex of rabbits, and their electroencephalographs (EEG) and behavior were observed in an unanesthetized and urestrained condition. A small amt. of penicillin (I) (0.002-0.004 ml. of 106 units/ml. soln.) was injected into the thalamus for making an **epileptogenic** focus, and its localization was confirmed after EEG recordings and behavioral observations. Localized sporadic spikes were produced from the I focus and they propagated to other regions of the brain. In this period, searching movements, oral behavior, and myoclonic jerks were observed. Elec. seizure discharges in all the leads were elicited 15-20 min. after I injection, and they subsided within 1-2 min., reappearing repeatedly at 2-5-min. intervals. Accompanied by these seizure discharges, behavioral changes such as restlessness, circling movements, head movements, mastication, generalized myoclonic or, rarely, clonic convulsions were displayed. Phenobarbital Na (20 mg./kg.) **inhibited** the EEG as well as behavioral changes, whereas diphenylhydantoin and trimethadione (100-150 mg./kg.) were ineffective. Nitrazepam and diazepam (both 2 mg./kg.) effectively suppressed the behavioral changes without eliminating the EEG seizures, indicating a distinct assocn. of the electroclin. phenomena. Sporadic spikes were generally resistant to all the drugs tested.
IT **57-30-7**
RL: BIOL (Biological study)
(brain electroactivity in response to)
RN 57-30-7 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl-, monosodium salt (9CI) (CA INDEX NAME)



● Na

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=> s l4/thu
FIELD CODES CANNOT BE CHANGED HERE
You may have tried to apply a field code to a term that already has a
field code.  You can only add a field code to a term that has no field
code appended to it.

=> s l3/thu
        187950 L3
        502933 THU/RL
L19      17212 L3/THU
                (L3 (L) THU/RL)

=> d his

     (FILE 'HOME' ENTERED AT 16:18:17 ON 16 APR 2003)

     FILE 'REGISTRY' ENTERED AT 16:18:23 ON 16 APR 2003
L1              STRUCTURE UPLOADED
L2             50 S L1 SSS SAM
L3         248167 S L1 SSS FUL

     FILE 'CAPLUS' ENTERED AT 16:19:09 ON 16 APR 2003
L4         187950 S L3
L5           1844 S EPILEPTOGEN?
L6             63 S L4 AND L5
L7          21745 S CONVUL?
L8           1642 S L4 AND L7
L9        3042475 S TREAT? OR THERAP?
L10          4089 S L9(P)L7
L11           336 S L4 AND L10
L12       1563686 S INHIBIT?
L13            23 S L6 AND L12
L14           110 S L10(L)L4
L15           122 S CONVULS? DISORDER?
L16             0 S L4(L)L15
L17            10 S L4 AND L15

     FILE 'STNGUIDE' ENTERED AT 16:33:30 ON 16 APR 2003

     FILE 'CAPLUS' ENTERED AT 16:33:36 ON 16 APR 2003
L18           110 S L4(L)L7(L)L9
L19         17212 S L3/THU

=> s l19 and l10
L20           64 L19 AND L10

=> d l20 1-64 bib,ab,hitstr
```
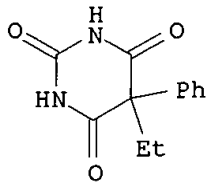
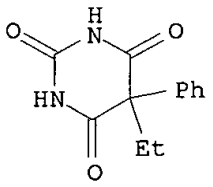

L20 ANSWER 1 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 2002:601654 CAPLUS
DN 138:231601
TI Interaction of the neurosteroid alphaxalone with conventional antiepileptic drugs in different types of experimental seizures
AU Borowicz, Kinga K.; Zadrozniak, Marek; Swiader, Mariusz; Kowalska, Aneta; Kleinrok, Zdzislaw; Czuczwar, Stanislaw J.
CS Department of Pathophysiology, Medical University, Lublin, 20-090, Pol.
SO European Journal of Pharmacology (2002), 449(1-2), 85-90
CODEN: EJPHAZ; ISSN: 0014-2999
PB Elsevier Science B.V.
DT Journal
LA English
AB A no. of neurosteroids exert antiseizure and/or neuroprotective properties. The aim of this study was to evaluate the effect of the neurosteroid alphaxalone on the protective action of conventional antiepileptics in four seizure tests. Alphaxalone (up to 5 mg/kg) did not exert a significant action against amygdala-kindled seizures in rats, or against pentetrazole- or aminophylline-induced **convulsions** in mice. The neuroactive steroid at the dose of 2.5 mg/kg significantly raised the threshold for electroconvulsions in mice. At 2.5 mg/kg, alphaxalone diminished the protective activity of valproate against maximal electroshock and at 2.5-5 mg/kg against pentetrazole-induced seizures in mice. However, alphaxalone (2.5 mg/kg) did not affect the protective activity of carbamazepine, diphenylhydantoin, phenobarbital or clonazepam against maximal electroshock and at 5 mg/kg did not affect that of phenobarbital, clonazepam and ethosuximide against pentetrazole-induced **convulsions**. Insignificant results were also obtained in the case of co-administration of alphaxalone with phenobarbital, valproate, clonazepam and carbamazepine against aminophylline-evoked seizures in mice. Also, in the kindling model of epilepsy, combinations of the neuroactive steroid (2.5 mg/kg) with valproate, carbamazepine, phenobarbital, diphenylhydantoin or clonazepam at their subprotective doses did not result in pro- or anticonvulsant activity. Valproate (284 mg/kg; the dose used in combination with alphaxalone) produced significant memory deficits in mice. Alphaxalone (2.5 mg/kg), valproate (at its ED50 value of 226 mg/kg) and the combination of valproate (284 mg/kg) with alphaxalone (2.5 mg/kg) did not affect long-term memory, evaluated in the passive avoidance task with mice. Alphaxalone administered alone or in combination with valproate caused no motor impairment in exptl. animals. Finally, alphaxalone (2.5 and 5 mg/kg) significantly increased the free plasma levels of valproate, strongly indicating that the neuroactive steroid-induced redn. of the protective activity of valproate is not related to pharmacokinetic phenomena. Summing up, alphaxalone does not seem to be a promising candidate for adjunctive **treatment** of epilepsy.
IT **50-06-6**, Phenobarbital, biological studies
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(interaction of the neurosteroid alphaxalone with conventional antiepileptic drugs in different types of exptl. seizures)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)



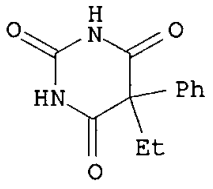
RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 2 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 2002:339487 CAPLUS
DN 137:345933
TI Niguldipine impairs the protective activity of carbamazepine and phenobarbital in amygdala-kindled seizures in rats
AU Borowicz, Kinga K.; Kleinrok, Zdzislaw; Czuczwar, Stanislaw J.
CS Department of Pathophysiology, Lublin Medical University, Lublin, 20-090, Pol.
SO European Neuropsychopharmacology (2002), 12(3), 225-233
CODEN: EURNE8; ISSN: 0924-977X
PB Elsevier Science B.V.
DT Journal
LA English
AB There is evidence that some calcium (Ca2+) channel inhibitors enhance the protective activity of antiepileptic drugs. Since clin. trials have not provided consistent data on this issue, the objective of this study was to evaluate the interaction of a dihydropyridine, niguldipine, with conventional antiepileptics in amygdala-kindled rats. Niguldipine (at 7.5 but not at 5 mg/kg) displayed a significant anticonvulsant effect, as regards seizure and afterdischarge durations in amygdala-kindled **convulsions** in rats, a model of complex partial seizures. No protective effect was obsd. when niguldipine (5 mg/kg) was combined with antiepileptics at subeffective doses, i.e. valproate (75 mg/kg), diphenylhydantoin (40 mg/kg), or clonazepam (0.003 mg/kg). Unexpectedly, the combined **treatment** of niguldipine (5 mg/kg) with carbamazepine (20 mg/kg) or phenobarbital (20 mg/kg) resulted in a proconvulsive action. BAY k-8644 (an L-type Ca2+ channel activator) did not modify the protective activity of niguldipine (7.5 mg/kg) or the opposite action of this dihydropyridine (5 mg/kg) in combinations with carbamazepine or phenobarbital. A pharmacokinetic interaction is not probable since niguldipine did not affect the free plasma levels of the antiepileptics. These data indicate that the opposite actions of niguldipine alone or combined with carbamazepine (or phenobarbital) were not assocd. with Ca2+ channel blockade. The present results may argue against the use of niguldipine as an adjuvant antiepileptic or for cardiovascular reasons in patients with complex partial seizures.
IT **50-06-6**, Phenobarbital, biological studies
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(niguldipine impairs the protective activity of carbamazepine and phenobarbital in amygdala-kindled seizures in rats)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)



RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 3 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 2002:127957 CAPLUS
DN 137:179715
TI Enhanced anticonvulsant activity of neuroactive steroids in a rat model of catamenial epilepsy
AU Reddy, Doodipala S.; Rogawski, Michael A.
CS Neuronal Excitability Section, Epilepsy Research Branch, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD, 20892-1408, USA
SO Epilepsia (2001), 42(3), 337-344
CODEN: EPILAK; ISSN: 0013-9580
PB Blackwell Science, Inc.
DT Journal
LA English
AB Perimenstrual catamenial epilepsy may in part be due to withdrawal of the endogenous progesterone-derived neurosteroid allopregnanolone that potentiates GABAA receptor-mediated inhibition. This work sought to det. whether the anticonvulsant potencies of neuroactive steroids, benzodiazepines, phenobarbital (PB), and valproate (VPA) are altered during the heightened seizure susceptibility accompanying neurosteroid withdrawal in a rat model of perimenstrual catamenial epilepsy. The drugs were evaluated for their ability to alter the **convulsant** activity of pentylenetetrazole (PTZ) in young adult female rats, in pseudopregnant rats with prolonged exposure to high levels of progesterone (and its neurosteroid metabolites), and in pseudopregnant rats 24 h after acute removal of neurosteroids by **treatment** with the 5.alpha.-reductase inhibitor finasteride. The drugs were administered at doses equiv. to twice their ED50 values for protection against PTZ-induced clonic seizures in naive young adult female rats. The anticonvulsant activities of allopregnanolone (5 mg/kg, s.c.), pregnanolone (5 mg/kg, s.c.), allotetrahydrodeoxycorticosterone (15 mg/kg, s.c.), and tetrahydrodeoxycorticosterone (10 mg/kg, s.c.) were enhanced by 34-127% after neurosteroid removal. The anticonvulsant activity of PB (65 mg/kg, i.p.) was also enhanced by 24% in neurosteroid-withdrawn animals. In contrast, the anticonvulsant activities of diazepam (4 mg/kg, i.p.), bretazenil (0.106 mg/kg, i.p.), and VPA (560 mg/kg, i.p.) were reduced or unchanged in neurosteroid-withdrawn animals. Thus, the anticonvulsant activity of neuroactive steroids is potentiated after neurosteroid removal, supporting the use of such agents in the **treatment** of perimenstrual catamenial epilepsy.
IT **50-06-6**, Phenobarbital, biological studies
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(anticonvulsant activity of neuroactive steroids and other compds. in a model of catamenial epilepsy)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)



L20 ANSWER 4 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 2002:113845 CAPLUS
DN 136:167382
TI Preparation of quinazolines as adenosine uptake inhibitors
IN Sasho, Setsuya; Komatsu, Kazunori; Kobayashi, Yumiko; Nonaka, Hiromi
PA Kyowa Hakko Kogyo Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 67 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2002047287	A2	20020212	JP 2001-153154	20010522
PRAI JP 2000-154603	A	20000525		

OS MARPAT 136:167382
AB Title compds. I [R1-R4 = H, formamide, halo, NH2, NO2, cyano, etc.; WV = NR5CO, N:CR6, CO, CH2; R5 = H, (un)substituted lower alkyl, aralkyl; R6 = H, (un)substituted lower alkyl, alkenyl, aryl, aralkyl; X = (CH2)mNR5, (un)substituted divalent pyrrolidine, piperidine, etc.,; m = 2-4; Y = O, S, NR7, two H; R7 = H, (un)substituted lower alkyl, aralkyl, alkoxycarbonyl, etc.; Z = (un)substituted Ph, 2-oxo-2,3-dihydro-1H-benzimidazol-5-yl; 2-thioxo-2,3-dihydro-1H-benzimidazol-5-yl] or their pharmaceutically acceptable salts are prepd. The compds. are useful for **treatment** of myocardial disease, cerebral ischemia, nephritis, diabetic nephropathy, pancreatitis, pain, **convulsion**. 1,6-Dimethyl-3-(piperidin-4-yl)-1,2,3,4-tetrahydro-2,4-dioxoquinazoline was reacted with 3,4-diethoxybenzoic acid in CH2Cl2 in the presence of Et3N, 1-hydroxybenzotriazole, and WSC HCl at room temp. for 18 h to give 83% 3-[1-(3,4-diethoxybenzoyl)piperidin-4-yl]-1,6-dimethyl-1,2,3,4-tetrahydro-2,4-dioxoquinazoline showing good adenosine uptake inhibitory activity in vitro.
IT **396650-68-3P 396650-73-0P 396650-76-3P**
396650-77-4P 396650-78-5P 396650-83-2P
396650-84-3P 396650-85-4P 396650-87-6P
396650-89-8P 396650-90-1P 396650-91-2P
396650-92-3P 396650-97-8P 396650-98-9P
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396651-17-5P 396651-18-6P 396651-38-0P
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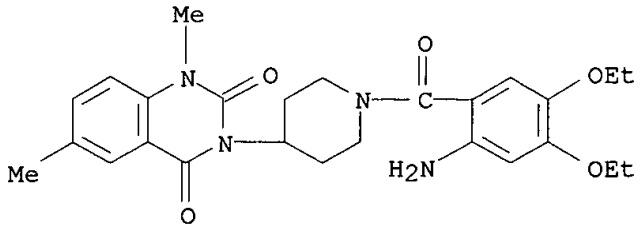
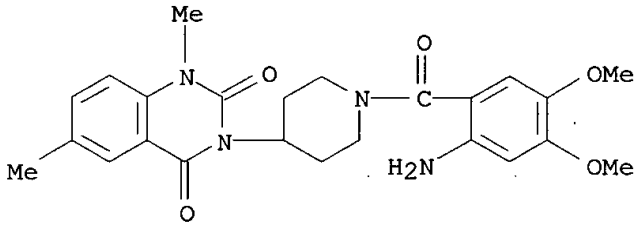
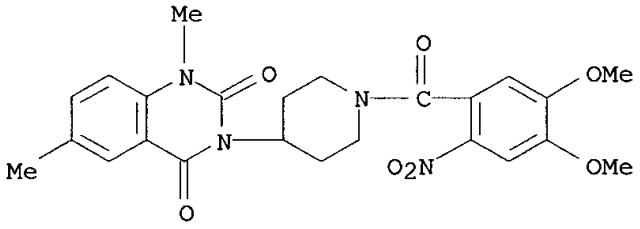
396651-47-1P 396651-49-3P 396651-50-6P
396651-52-8P 396651-55-1P 396651-57-3P
396651-59-5P 396651-60-8P 396651-63-1P
396651-64-2P 396651-66-4P 396651-67-5P
396651-69-7P 396651-70-0P 396651-73-3P
396651-74-4P 396651-75-5P 396651-78-8P
396651-80-2P 396651-81-3P 396651-83-5P
396651-84-6P 396652-00-9P 396652-04-3P
396652-10-1P 396652-11-2P 396652-16-7P
396652-17-8P 396652-18-9P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of)
RN 396650-68-3 CAPLUS
CN Piperidine, 1-(2-amino-4,5-diethoxybenzoyl)-4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)- (9CI) (CA INDEX NAME)



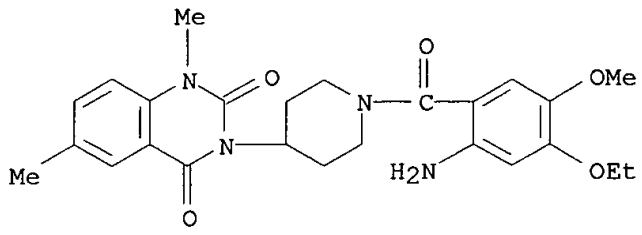
RN 396650-73-0 CAPLUS
CN Piperidine, 1-(2-amino-4,5-dimethoxybenzoyl)-4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)- (9CI) (CA INDEX NAME)



RN 396650-76-3 CAPLUS
CN Piperidine, 4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-(4,5-dimethoxy-2-nitrobenzoyl)- (9CI) (CA INDEX NAME)

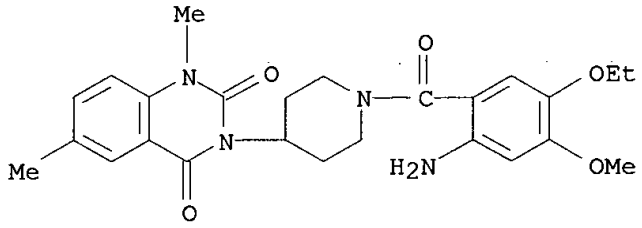


RN 396650-77-4 CAPLUS
CN Piperidine, 1-(2-amino-4-ethoxy-5-methoxybenzoyl)-4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-, monohydrochloride (9CI) (CA INDEX NAME)



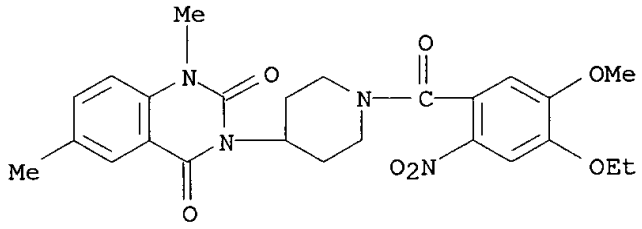
● HCl

RN 396650-78-5 CAPLUS
CN Piperidine, 1-(2-amino-5-ethoxy-4-methoxybenzoyl)-4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-, monohydrochloride (9CI) (CA INDEX NAME)

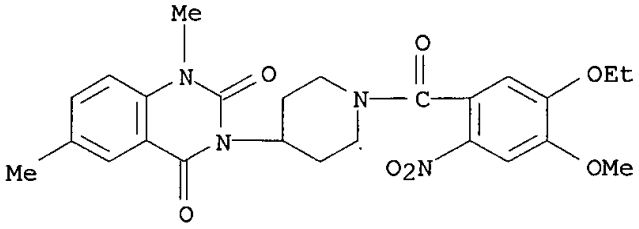


● HCl

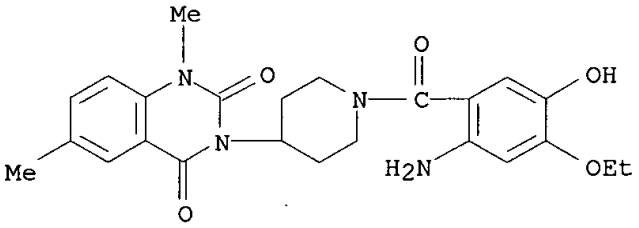
RN 396650-83-2 CAPLUS
CN Piperidine, 4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-(4-ethoxy-5-methoxy-2-nitrobenzoyl)- (9CI) (CA INDEX NAME)



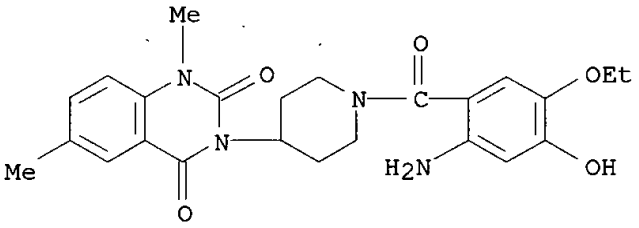
RN 396650-84-3 CAPLUS
CN Piperidine, 4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-(5-ethoxy-4-methoxy-2-nitrobenzoyl)- (9CI) (CA INDEX NAME)



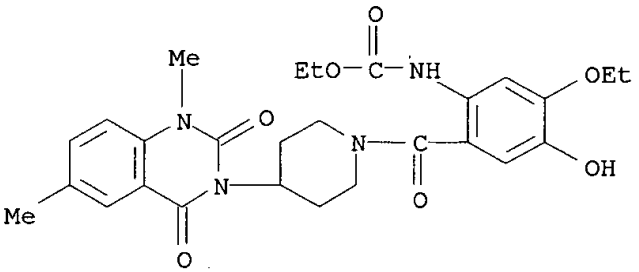
RN 396650-85-4 CAPLUS
CN Piperidine, 1-(2-amino-4-ethoxy-5-hydroxybenzoyl)-4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)- (9CI) (CA INDEX NAME)



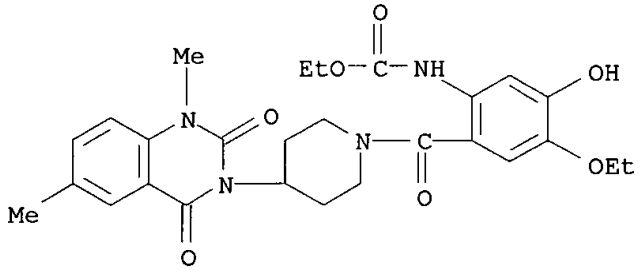
RN 396650-87-6 CAPLUS
CN Piperidine, 1-(2-amino-5-ethoxy-4-hydroxybenzoyl)-4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)- (9CI) (CA INDEX NAME)



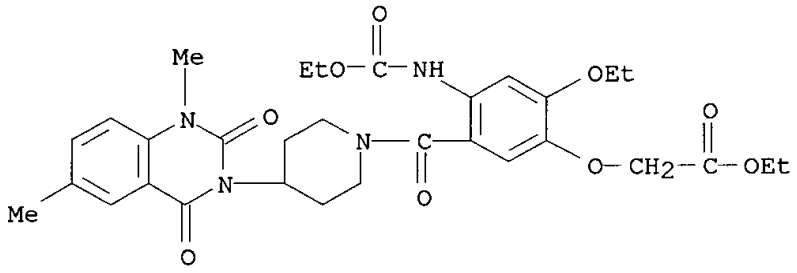
RN 396650-89-8 CAPLUS
CN Carbamic acid, [2-[[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-5-ethoxy-4-hydroxyphenyl]-, ethyl ester (9CI) (CA INDEX NAME)



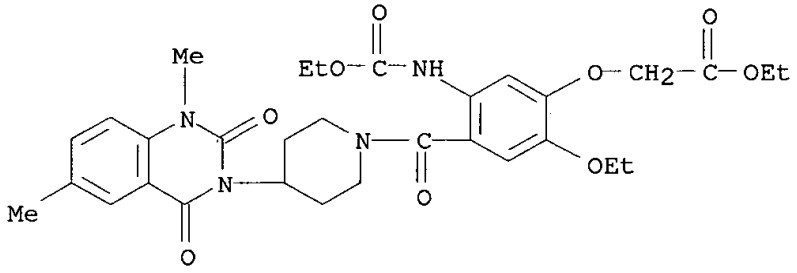
RN 396650-90-1 CAPLUS
CN Carbamic acid, [2-[[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-4-ethoxy-5-hydroxyphenyl]-, ethyl ester (9CI) (CA INDEX NAME)



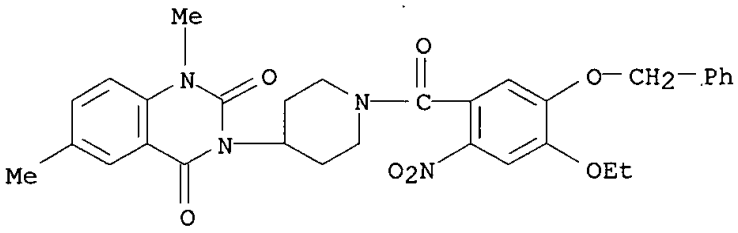
RN 396650-91-2 CAPLUS
CN Acetic acid, [5-[[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-2-ethoxy-4-[(ethoxycarbonyl)amino]phenoxy]-, ethyl ester (9CI) (CA INDEX NAME)



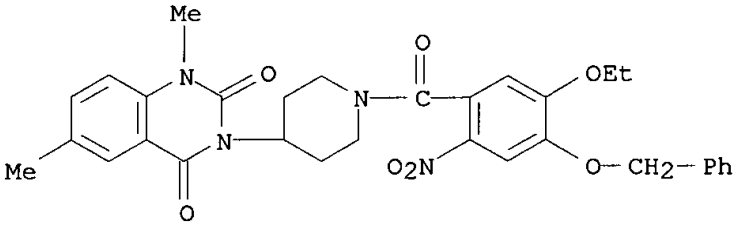
RN 396650-92-3 CAPLUS
CN Acetic acid, [4-[[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-2-ethoxy-5-[(ethoxycarbonyl)amino]phenoxy]-, ethyl ester (9CI) (CA INDEX NAME)



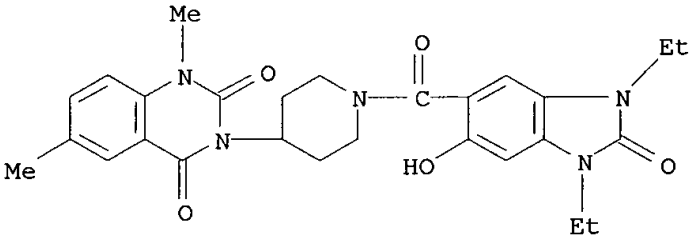
RN 396650-97-8 CAPLUS
CN Piperidine, 4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-[4-ethoxy-2-nitro-5-(phenylmethoxy)benzoyl]- (9CI) (CA INDEX NAME)



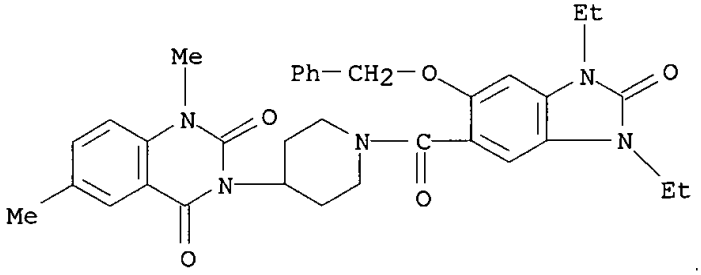
RN 396650-98-9 CAPLUS
CN Piperidine, 4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-[5-ethoxy-2-nitro-4-(phenylmethoxy)benzoyl]- (9CI) (CA INDEX NAME)



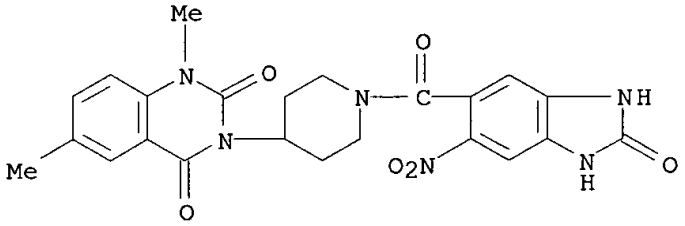
RN 396651-04-0 CAPLUS
CN Piperidine, 1-[(1,3-diethyl-2,3-dihydro-6-hydroxy-2-oxo-1H-benzimidazol-5-yl)carbonyl]-4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)- (9CI) (CA INDEX NAME)



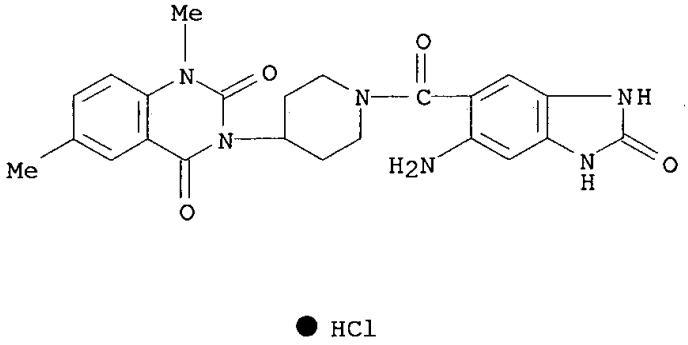
RN 396651-07-3 CAPLUS
CN Piperidine, 1-[[1,3-diethyl-2,3-dihydro-2-oxo-6-(phenylmethoxy)-1H-benzimidazol-5-yl]carbonyl]-4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)- (9CI) (CA INDEX NAME)



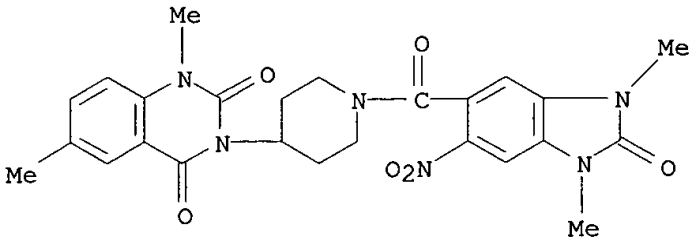
RN 396651-09-5 CAPLUS
CN Piperidine, 4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-[(2,3-dihydro-6-nitro-2-oxo-1H-benzimidazol-5-yl)carbonyl]- (9CI) (CA INDEX NAME)



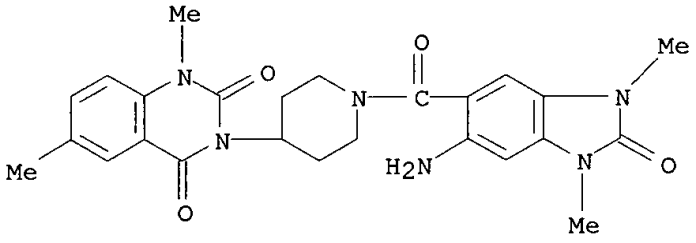
RN 396651-10-8 CAPLUS
CN Piperidine, 1-[(6-amino-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl)carbonyl]-4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-, monohydrochloride (9CI) (CA INDEX NAME)



RN 396651-12-0 CAPLUS
CN Piperidine, 4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-[(2,3-dihydro-1,3-dimethyl-6-nitro-2-oxo-1H-benzimidazol-5-yl)carbonyl]- (9CI) (CA INDEX NAME)

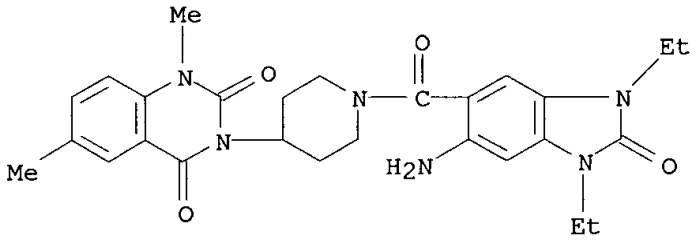


RN 396651-13-1 CAPLUS
CN Piperidine, 1-[(6-amino-2,3-dihydro-1,3-dimethyl-2-oxo-1H-benzimidazol-5-yl)carbonyl]-4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-, monohydrochloride (9CI) (CA INDEX NAME)



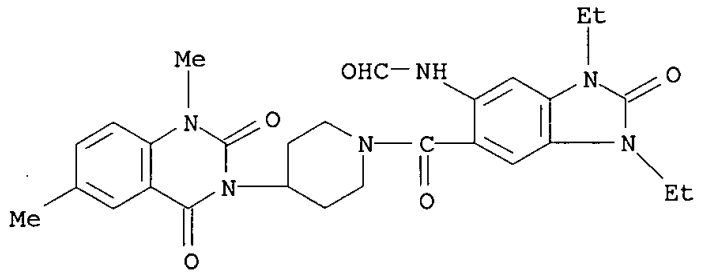
● HCl

RN 396651-17-5 CAPLUS
CN Piperidine, 1-[(6-amino-1,3-diethyl-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl)carbonyl]-4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-, monohydrochloride (9CI) (CA INDEX NAME)

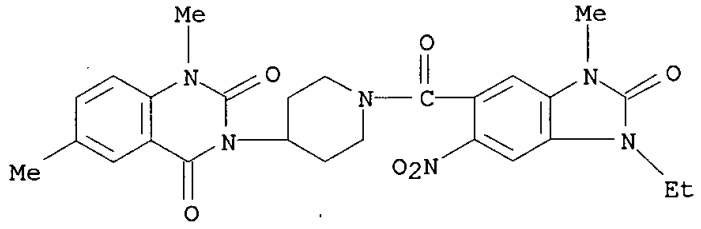


● HCl

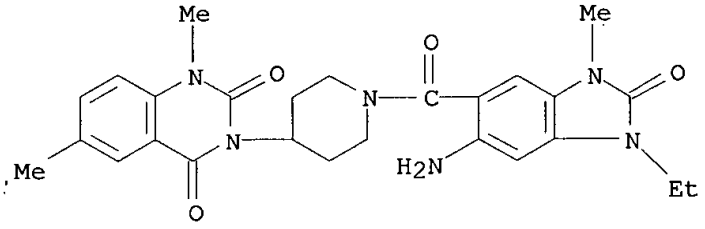
RN 396651-18-6 CAPLUS
CN Piperidine, 1-[[1,3-diethyl-6-(formylamino)-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl]carbonyl]-4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)- (9CI) (CA INDEX NAME)



RN 396651-38-0 CAPLUS
CN Piperidine, 4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-[(1-ethyl-2,3-dihydro-3-methyl-6-nitro-2-oxo-1H-benzimidazol-5-yl)carbonyl]- (9CI) (CA INDEX NAME)

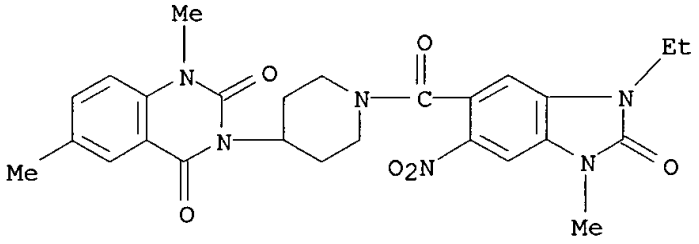


RN 396651-39-1 CAPLUS
CN Piperidine, 1-[(6-amino-1-ethyl-2,3-dihydro-3-methyl-2-oxo-1H-benzimidazol-5-yl)carbonyl]-4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-, monohydrochloride (9CI) (CA INDEX NAME)

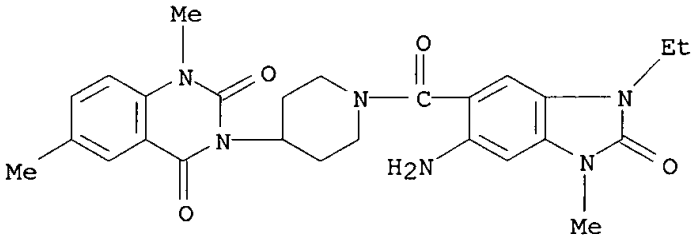


● HCl

RN 396651-42-6 CAPLUS
CN Piperidine, 4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-[(3-ethyl-2,3-dihydro-1-methyl-6-nitro-2-oxo-1H-benzimidazol-5-yl)carbonyl]- (9CI) (CA INDEX NAME)

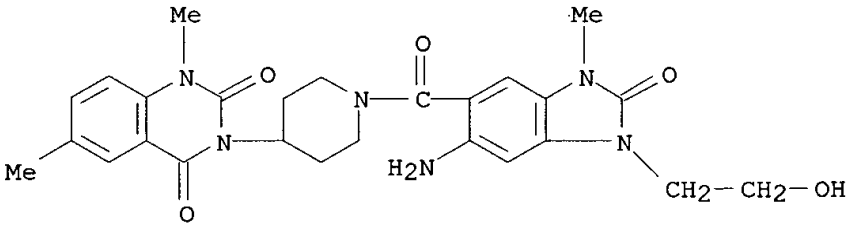


RN 396651-43-7 CAPLUS
CN Piperidine, 1-[(6-amino-3-ethyl-2,3-dihydro-1-methyl-2-oxo-1H-benzimidazol-5-yl)carbonyl]-4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-, monohydrochloride (9CI) (CA INDEX NAME)

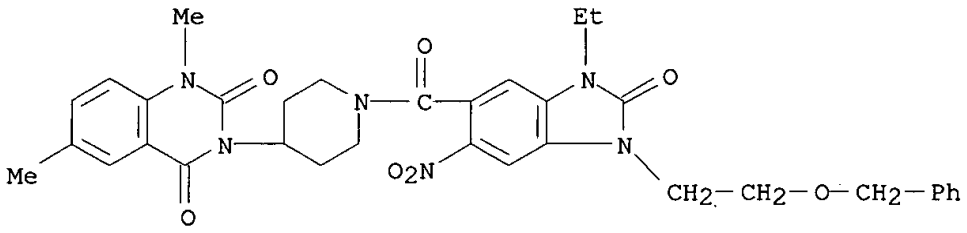


● HCl

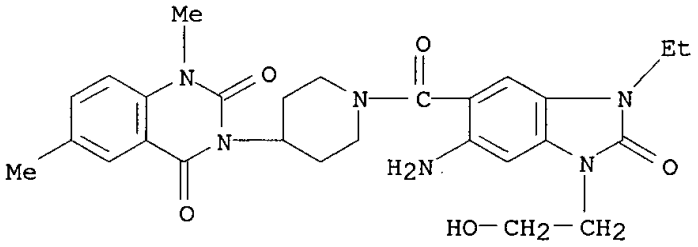
RN 396651-47-1 CAPLUS
CN Piperidine, 1-[[6-amino-2,3-dihydro-1-(2-hydroxyethyl)-3-methyl-2-oxo-1H-benzimidazol-5-yl]carbonyl]-4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)- (9CI) (CA INDEX NAME)



RN 396651-49-3 CAPLUS
CN Piperidine, 4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-[[3-ethyl-2,3-dihydro-6-nitro-2-oxo-1-[2-(phenylmethoxy)ethyl]-1H-benzimidazol-5-yl]carbonyl]- (9CI) (CA INDEX NAME)

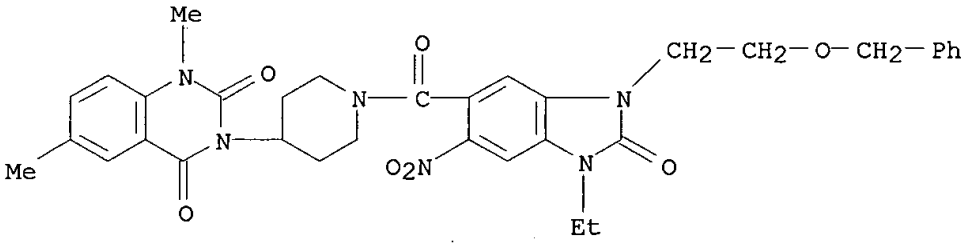


RN 396651-50-6 CAPLUS
CN Piperidine, 1-[[6-amino-3-ethyl-2,3-dihydro-1-(2-hydroxyethyl)-2-oxo-1H-benzimidazol-5-yl]carbonyl]-4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-, monohydrochloride (9CI) (CA INDEX NAME)

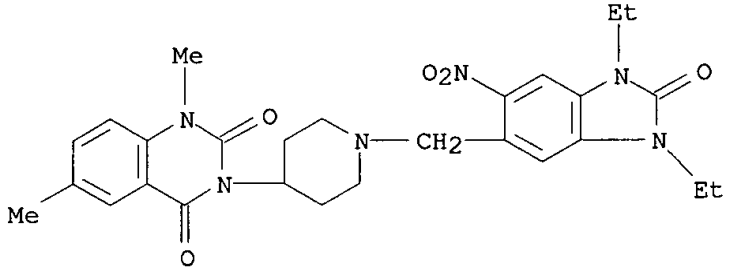


● HCl

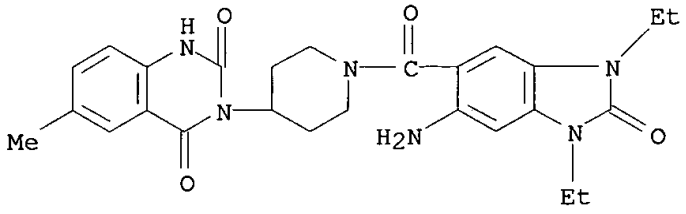
RN 396651-52-8 CAPLUS
CN Piperidine, 4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-[[1-ethyl-2,3-dihydro-6-nitro-2-oxo-3-[2-(phenylmethoxy)ethyl]-1H-benzimidazol-5-yl]carbonyl]- (9CI) (CA INDEX NAME)



RN 396651-55-1 CAPLUS
CN 2,4(1H,3H)-Quinazolinedione, 3-[1-[(1,3-diethyl-2,3-dihydro-6-nitro-2-oxo-1H-benzimidazol-5-yl)methyl]-4-piperidinyl]-1,6-dimethyl- (9CI) (CA INDEX NAME)

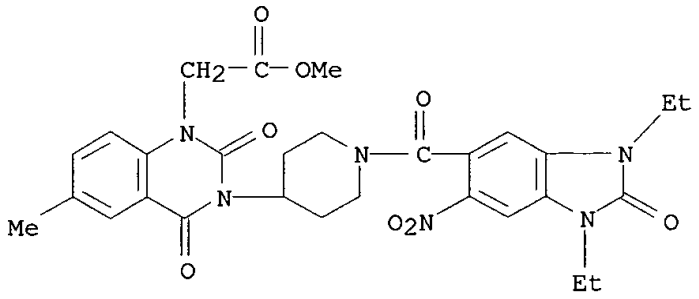


RN 396651-57-3 CAPLUS
CN Piperidine, 1-[(6-amino-1,3-diethyl-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl)carbonyl]-4-(1,4-dihydro-6-methyl-2,4-dioxo-3(2H)-quinazolinyl)-, monohydrochloride (9CI) (CA INDEX NAME)

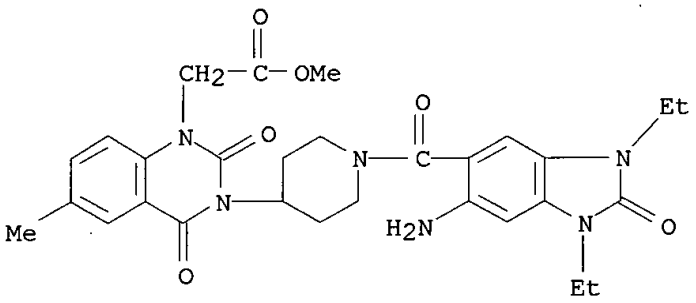


● HCl

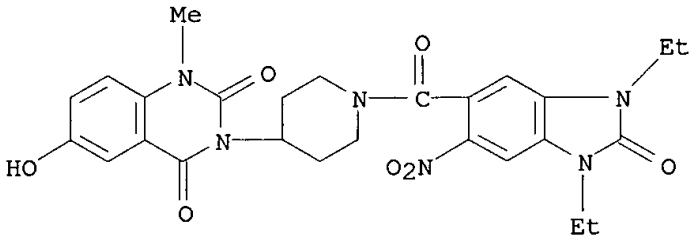
RN 396651-59-5 CAPLUS
CN 1(2H)-Quinazolineacetic acid, 3-[1-[(1,3-diethyl-2,3-dihydro-6-nitro-2-oxo-1H-benzimidazol-5-yl)carbonyl]-4-piperidinyl]-3,4-dihydro-6-methyl-2,4-dioxo-, methyl ester (9CI) (CA INDEX NAME)



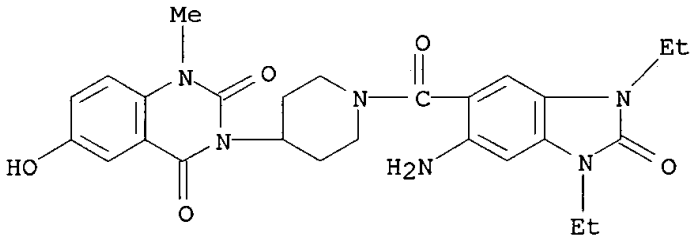
RN 396651-60-8 CAPLUS
CN 1(2H)-Quinazolineacetic acid, 3-[1-[(6-amino-1,3-diethyl-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl)carbonyl]-4-piperidinyl]-3,4-dihydro-6-methyl-2,4-dioxo-, methyl ester (9CI) (CA INDEX NAME)



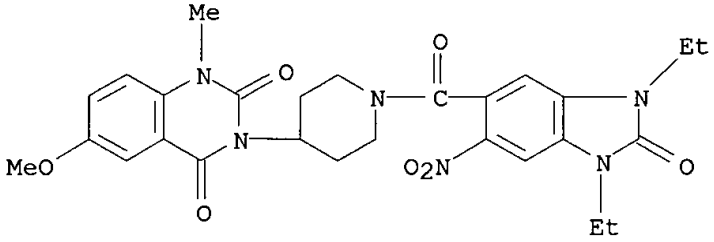
RN 396651-63-1 CAPLUS
CN Piperidine, 1-[(1,3-diethyl-2,3-dihydro-6-nitro-2-oxo-1H-benzimidazol-5-yl)carbonyl]-4-(1,4-dihydro-6-hydroxy-1-methyl-2,4-dioxo-3(2H)-quinazolinyl)- (9CI) (CA INDEX NAME)



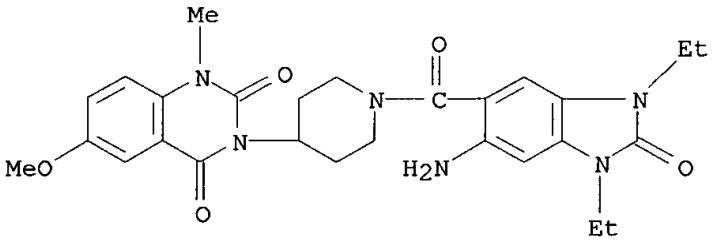
RN 396651-64-2 CAPLUS
CN Piperidine, 1-[(6-amino-1,3-diethyl-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl)carbonyl]-4-(1,4-dihydro-6-hydroxy-1-methyl-2,4-dioxo-3(2H)-quinazolinyl)- (9CI) (CA INDEX NAME)



RN 396651-66-4 CAPLUS
CN Piperidine, 1-[(1,3-diethyl-2,3-dihydro-6-nitro-2-oxo-1H-benzimidazol-5-yl)carbonyl]-4-(1,4-dihydro-6-methoxy-1-methyl-2,4-dioxo-3(2H)-quinazolinyl)- (9CI) (CA INDEX NAME)

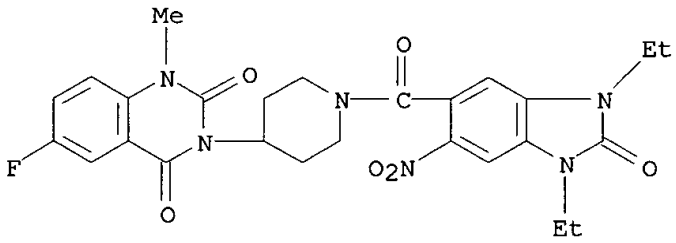


RN 396651-67-5 CAPLUS
CN Piperidine, 1-[(6-amino-1,3-diethyl-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl)carbonyl]-4-(1,4-dihydro-6-methoxy-1-methyl-2,4-dioxo-3(2H)-quinazolinyl)-, monohydrochloride (9CI) (CA INDEX NAME)

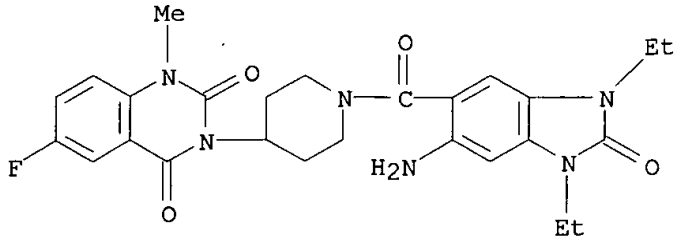


● HCl

RN 396651-69-7 CAPLUS
CN Piperidine, 1-[(1,3-diethyl-2,3-dihydro-6-nitro-2-oxo-1H-benzimidazol-5-yl)carbonyl]-4-(6-fluoro-1,4-dihydro-1-methyl-2,4-dioxo-3(2H)-quinazolinyl)- (9CI) (CA INDEX NAME)

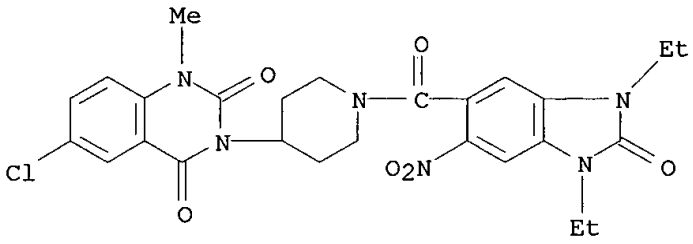


RN 396651-70-0 CAPLUS
CN Piperidine, 1-[(6-amino-1,3-diethyl-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl)carbonyl]-4-(6-fluoro-1,4-dihydro-1-methyl-2,4-dioxo-3(2H)-quinazolinyl)-, monohydrochloride (9CI) (CA INDEX NAME)

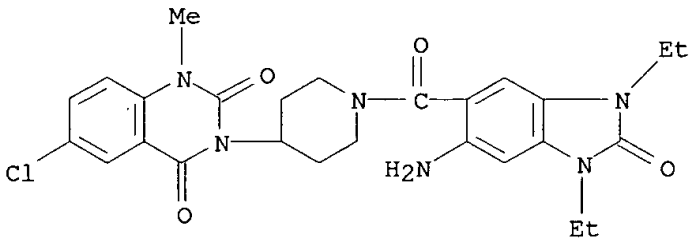


● HCl

RN 396651-73-3 CAPLUS
CN Piperidine, 4-(6-chloro-1,4-dihydro-1-methyl-2,4-dioxo-3(2H)-quinazolinyl)-1-[(1,3-diethyl-2,3-dihydro-6-nitro-2-oxo-1H-benzimidazol-5-yl)carbonyl]- (9CI) (CA INDEX NAME)

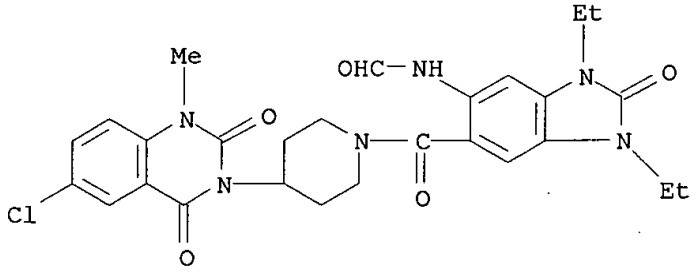


RN 396651-74-4 CAPLUS
CN Piperidine, 1-[(6-amino-1,3-diethyl-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl)carbonyl]-4-(6-chloro-1,4-dihydro-1-methyl-2,4-dioxo-3(2H)-quinazolinyl)-, monohydrochloride (9CI) (CA INDEX NAME)

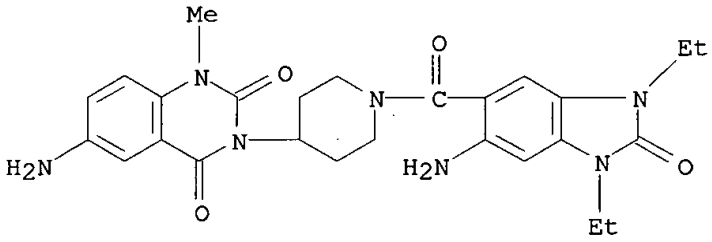


● HCl

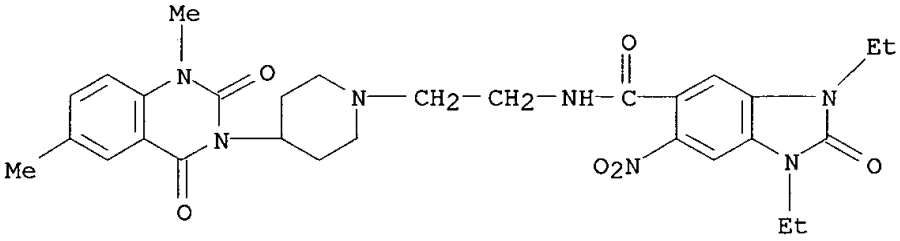
RN 396651-75-5 CAPLUS
CN Piperidine, 4-(6-chloro-1,4-dihydro-1-methyl-2,4-dioxo-3(2H)-quinazolinyl)-1-[[1,3-diethyl-6-(formylamino)-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl]carbonyl]- (9CI) (CA INDEX NAME)



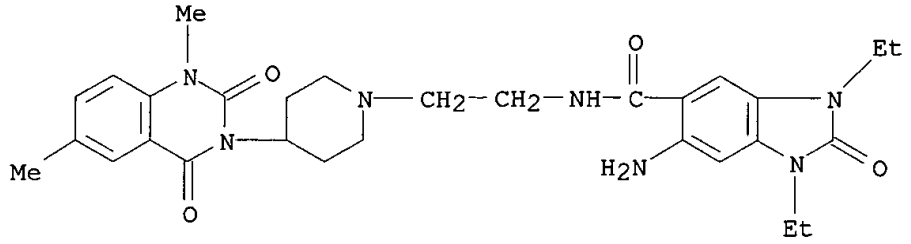
RN 396651-78-8 CAPLUS
CN Piperidine, 1-[(6-amino-1,3-diethyl-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl)carbonyl]-4-(6-amino-1,4-dihydro-1-methyl-2,4-dioxo-3(2H)-quinazolinyl)- (9CI) (CA INDEX NAME)



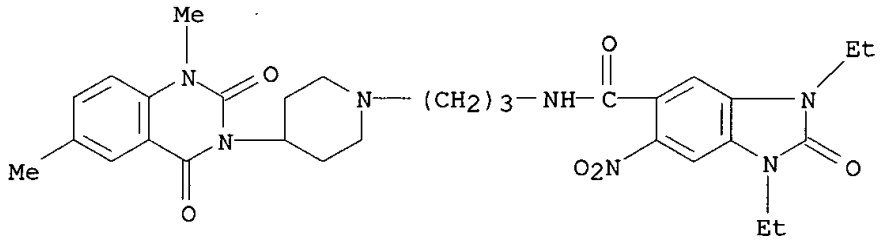
RN 396651-80-2 CAPLUS
CN 1H-Benzimidazole-5-carboxamide, N-[2-[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]ethyl]-1,3-diethyl-2,3-dihydro-6-nitro-2-oxo- (9CI) (CA INDEX NAME)



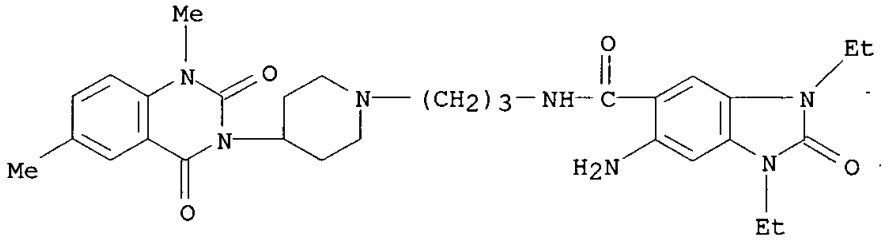
RN 396651-81-3 CAPLUS
CN 1H-Benzimidazole-5-carboxamide, 6-amino-N-[2-[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]ethyl]-1,3-diethyl-2,3-dihydro-2-oxo- (9CI) (CA INDEX NAME)



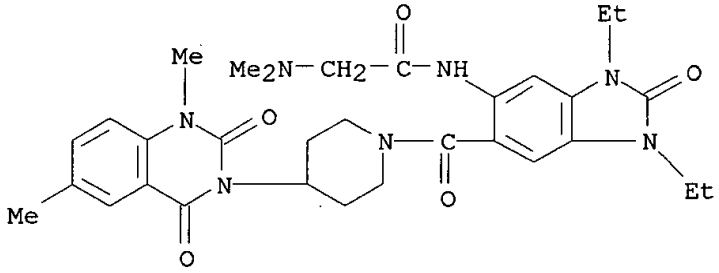
RN 396651-83-5 CAPLUS
CN 1H-Benzimidazole-5-carboxamide, N-[3-[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]propyl]-1,3-diethyl-2,3-dihydro-6-nitro-2-oxo- (9CI) (CA INDEX NAME)



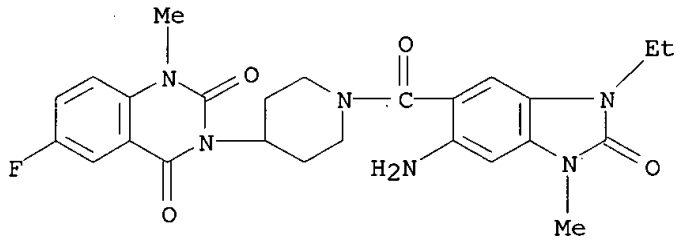
RN 396651-84-6 CAPLUS
CN 1H-Benzimidazole-5-carboxamide, 6-amino-N-[3-[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]propyl]-1,3-diethyl-2,3-dihydro-2-oxo- (9CI) (CA INDEX NAME)



RN 396652-00-9 CAPLUS
CN Acetamide, N-[6-[[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-1,3-diethyl-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl]-2-(dimethylamino)- (9CI) (CA INDEX NAME)

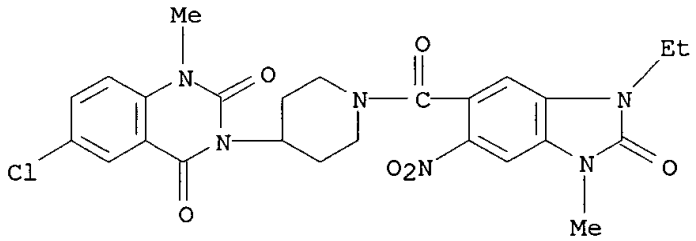


RN 396652-04-3 CAPLUS
CN Piperidine, 1-[(6-amino-3-ethyl-2,3-dihydro-1-methyl-2-oxo-1H-benzimidazol-5-yl)carbonyl]-4-(6-fluoro-1,4-dihydro-1-methyl-2,4-dioxo-3(2H)-quinazolinyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

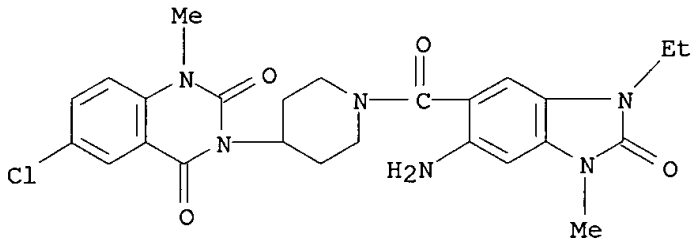
RN 396652-10-1 CAPLUS
CN Piperidine, 4-(6-chloro-1,4-dihydro-1-methyl-2,4-dioxo-3(2H)-quinazolinyl)-1-[(3-ethyl-2,3-dihydro-1-methyl-6-nitro-2-oxo-1H-benzimidazol-5-yl)carbonyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

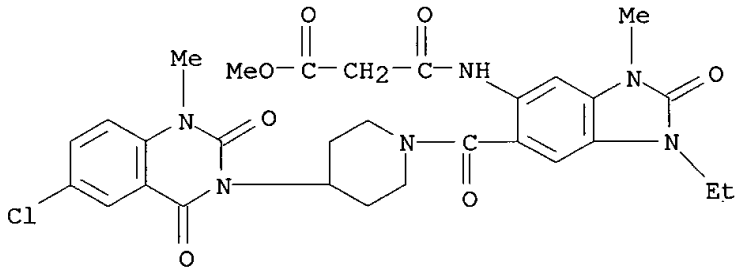
RN 396652-11-2 CAPLUS
CN Piperidine, 1-[(6-amino-3-ethyl-2,3-dihydro-1-methyl-2-oxo-1H-benzimidazol-5-yl)carbonyl]-4-(6-chloro-1,4-dihydro-1-methyl-2,4-dioxo-3(2H)-

quinazolinyl)-, monohydrochloride (9CI) (CA INDEX NAME)

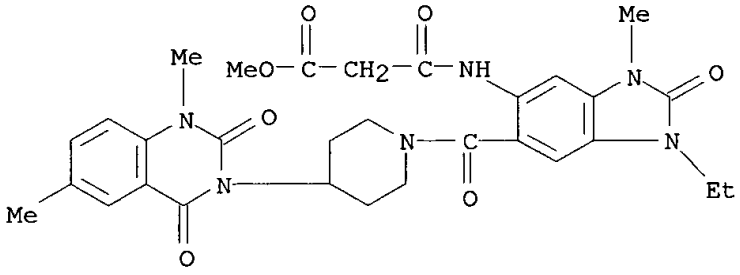


● HCl

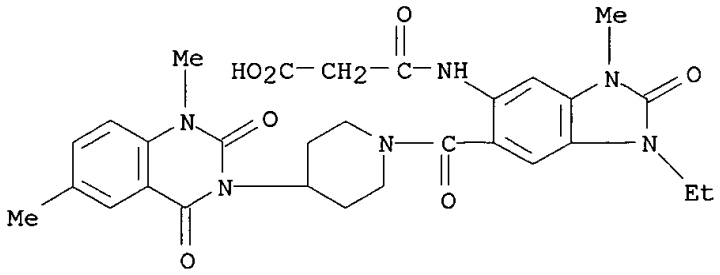
RN 396652-16-7 CAPLUS
CN Propanoic acid, 3-[[6-[[4-(6-chloro-1,4-dihydro-1-methyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-1-ethyl-2,3-dihydro-3-methyl-2-oxo-1H-benzimidazol-5-yl]amino]-3-oxo-, methyl ester (9CI) (CA INDEX NAME)



RN 396652-17-8 CAPLUS
CN Propanoic acid, 3-[[6-[[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-1-ethyl-2,3-dihydro-3-methyl-2-oxo-1H-benzimidazol-5-yl]amino]-3-oxo-, methyl ester (9CI) (CA INDEX NAME)



RN 396652-18-9 CAPLUS
CN Propanoic acid, 3-[[6-[[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-1-ethyl-2,3-dihydro-3-methyl-2-oxo-1H-benzimidazol-5-yl]amino]-3-oxo- (9CI) (CA INDEX NAME)



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396650-81-0P 396650-82-1P 396650-93-4P
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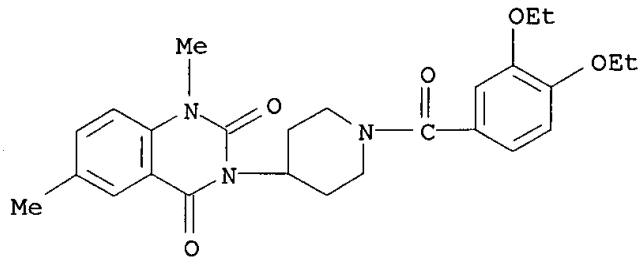
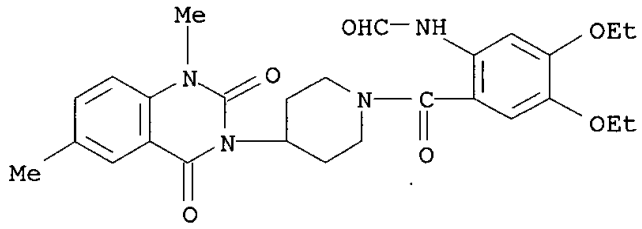
396652-20-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of)

RN 396650-67-2 CAPLUS

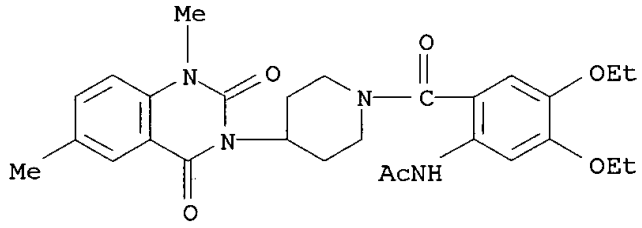
CN Piperidine, 1-(3,4-diethoxybenzoyl)-4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)- (9CI) (CA INDEX NAME)



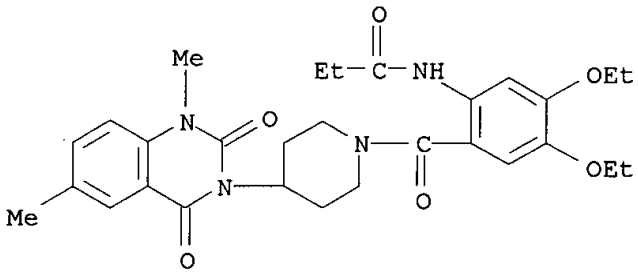
RN 396650-69-4 CAPLUS
CN Piperidine, 1-[4,5-diethoxy-2-(formylamino)benzoyl]-4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)- (9CI) (CA INDEX NAME)



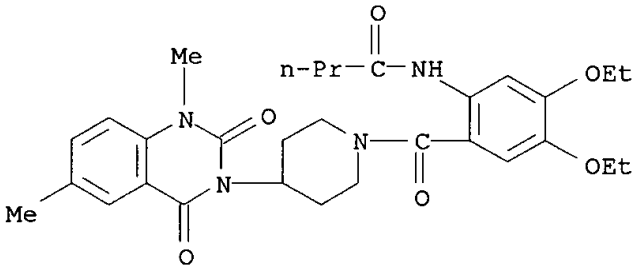
RN 396650-70-7 CAPLUS
CN Acetamide, N-[2-[[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-4,5-diethoxyphenyl]- (9CI) (CA INDEX NAME)



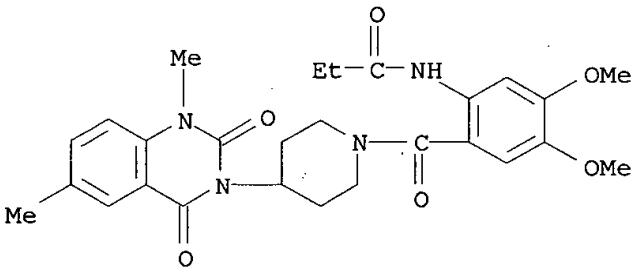
RN 396650-71-8 CAPLUS
CN Propanamide, N-[2-[[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-4,5-diethoxyphenyl]- (9CI) (CA INDEX NAME)



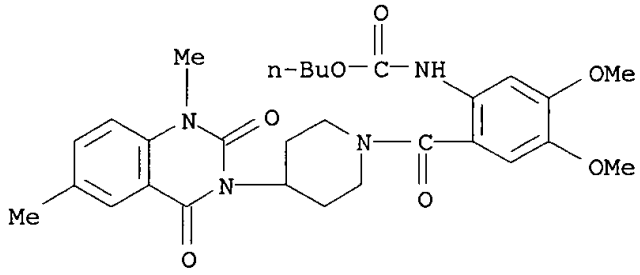
RN 396650-72-9 CAPLUS
CN Butanamide, N-[2-[[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-4,5-diethoxyphenyl]- (9CI) (CA INDEX NAME)



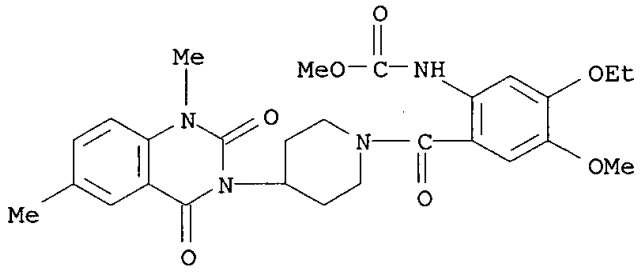
RN 396650-74-1 CAPLUS
CN Propanamide, N-[2-[[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-4,5-dimethoxyphenyl]- (9CI) (CA INDEX NAME)



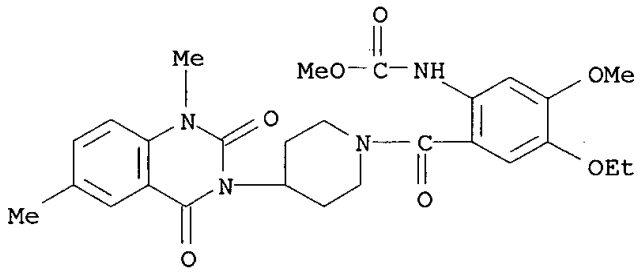
RN 396650-75-2 CAPLUS
CN Carbamic acid, [2-[[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-4,5-dimethoxyphenyl]-, butyl ester (9CI) (CA INDEX NAME)



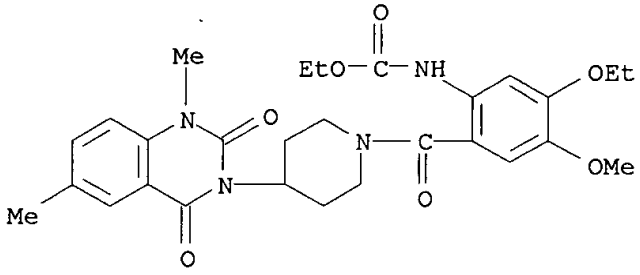
RN 396650-79-6 CAPLUS
CN Carbamic acid, [2-[[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-5-ethoxy-4-methoxyphenyl]-, methyl ester (9CI) (CA INDEX NAME)



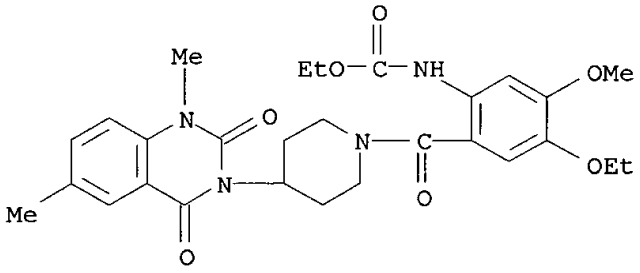
RN 396650-80-9 CAPLUS
CN Carbamic acid, [2-[[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-4-ethoxy-5-methoxyphenyl]-, methyl ester (9CI) (CA INDEX NAME)



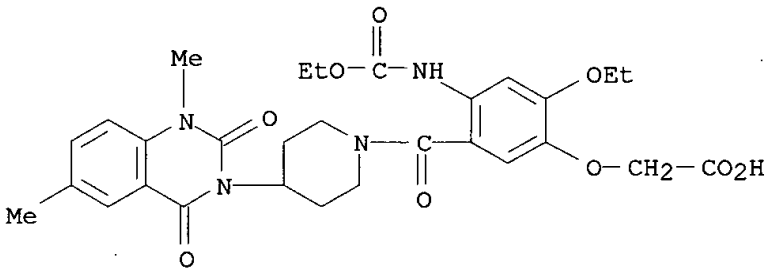
RN 396650-81-0 CAPLUS
CN Carbamic acid, [2-[[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-5-ethoxy-4-methoxyphenyl]-, ethyl ester (9CI) (CA INDEX NAME)



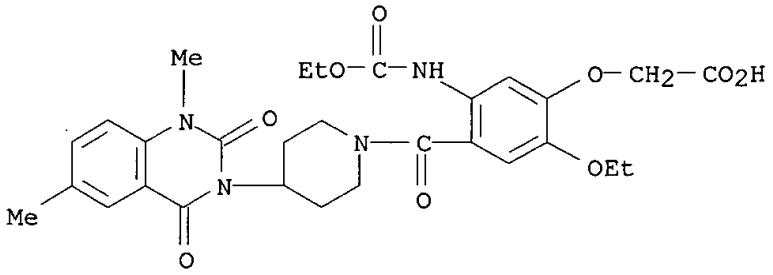
RN 396650-82-1 CAPLUS
CN Carbamic acid, [2-[[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-4-ethoxy-5-methoxyphenyl]-, ethyl ester (9CI) (CA INDEX NAME)



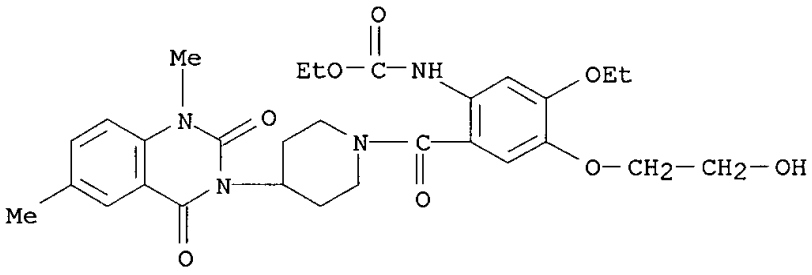
RN 396650-93-4 CAPLUS
CN Acetic acid, [5-[[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-2-ethoxy-4-[(ethoxycarbonyl)amino]phenoxy]- (9CI) (CA INDEX NAME)



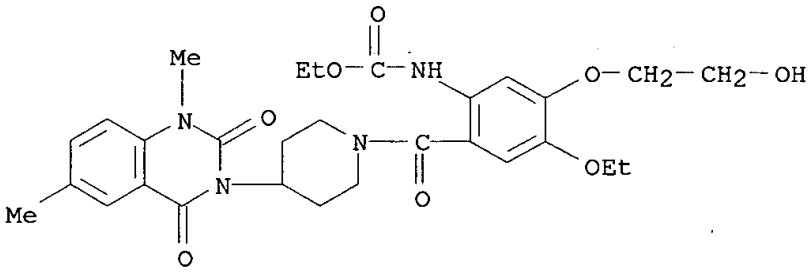
RN 396650-94-5 CAPLUS
CN Acetic acid, [4-[[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-2-ethoxy-5-[(ethoxycarbonyl)amino]phenoxy]- (9CI) (CA INDEX NAME)



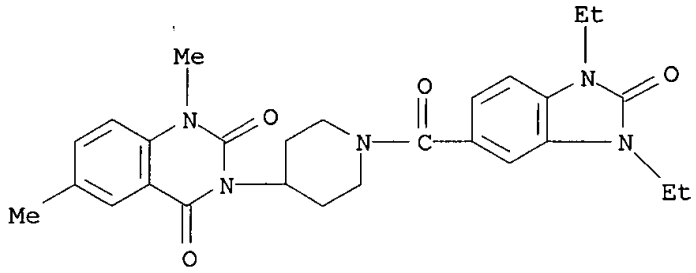
RN 396650-95-6 CAPLUS
CN Carbamic acid, [2-[[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-5-ethoxy-4-(2-hydroxyethoxy)phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



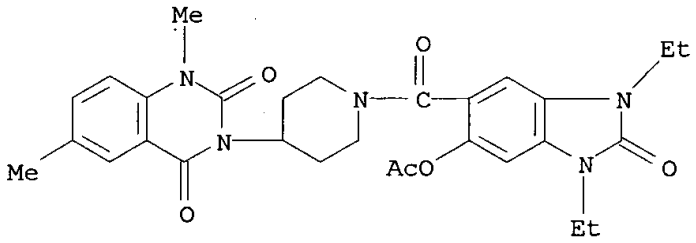
RN 396650-96-7 CAPLUS
CN Carbamic acid, [2-[[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-4-ethoxy-5-(2-hydroxyethoxy)phenyl]-, ethyl ester (9CI) (CA INDEX NAME)



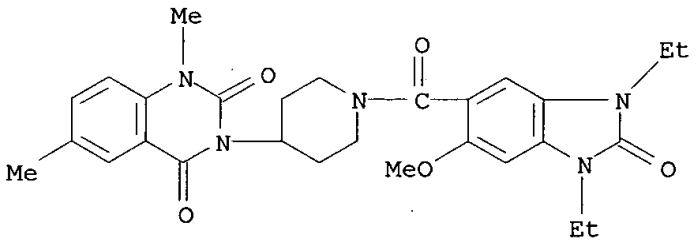
RN 396651-03-9 CAPLUS
CN Piperidine, 1-[(1,3-diethyl-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl)carbonyl]-4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-(9CI) (CA INDEX NAME)



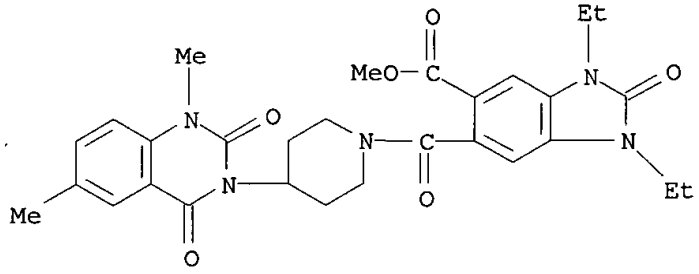
RN 396651-05-1 CAPLUS
CN Piperidine, 1-[[6-(acetyloxy)-1,3-diethyl-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl]carbonyl]-4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)- (9CI) (CA INDEX NAME)



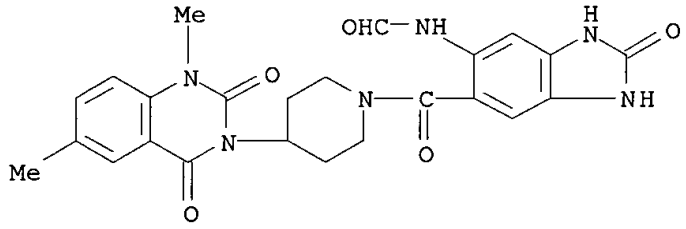
RN 396651-06-2 CAPLUS
CN Piperidine, 1-[(1,3-diethyl-2,3-dihydro-6-methoxy-2-oxo-1H-benzimidazol-5-yl)carbonyl]-4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)- (9CI) (CA INDEX NAME)



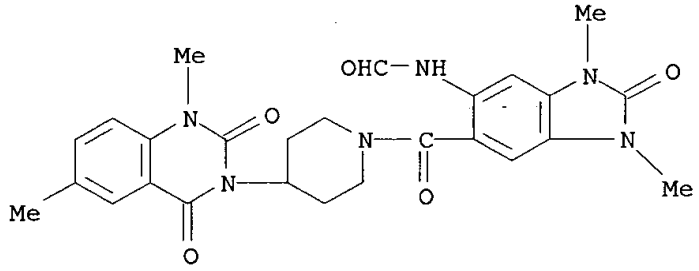
RN 396651-08-4 CAPLUS
CN 1H-Benzimidazole-5-carboxylic acid, 6-[[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-1,3-diethyl-2,3-dihydro-2-oxo-, methyl ester (9CI) (CA INDEX NAME)



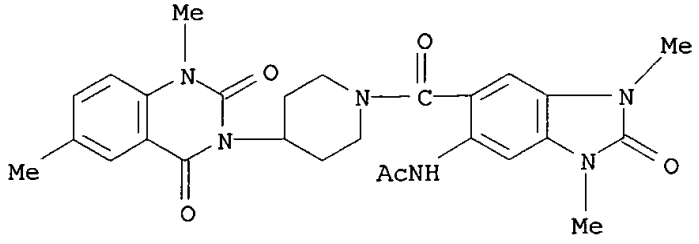
RN 396651-11-9 CAPLUS
CN Piperidine, 4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-[[6-(formylamino)-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl]carbonyl]- (9CI) (CA INDEX NAME)



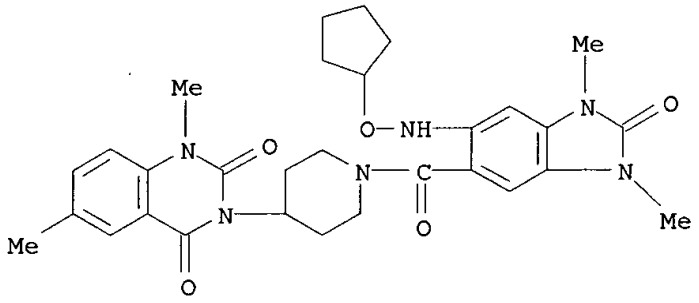
RN 396651-14-2 CAPLUS
CN Piperidine, 4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-[[6-(formylamino)-2,3-dihydro-1,3-dimethyl-2-oxo-1H-benzimidazol-5-yl]carbonyl]- (9CI) (CA INDEX NAME)



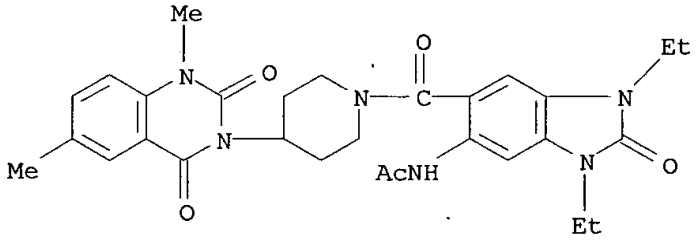
RN 396651-15-3 CAPLUS
CN Acetamide, N-[6-[[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-2,3-dihydro-1,3-dimethyl-2-oxo-1H-benzimidazol-5-yl]- (9CI) (CA INDEX NAME)



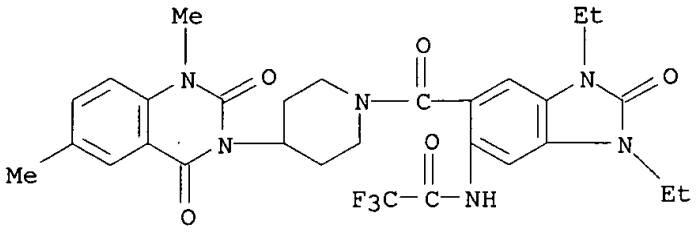
RN 396651-16-4 CAPLUS
CN Piperidine, 1-[[6-[(cyclopentyloxy)amino]-2,3-dihydro-1,3-dimethyl-2-oxo-1H-benzimidazol-5-yl]carbonyl]-4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)- (9CI) (CA INDEX NAME)



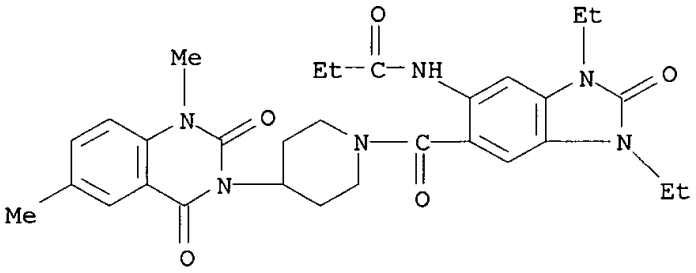
RN 396651-19-7 CAPLUS
CN Acetamide, N-[6-[[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-1,3-diethyl-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl]- (9CI) (CA INDEX NAME)



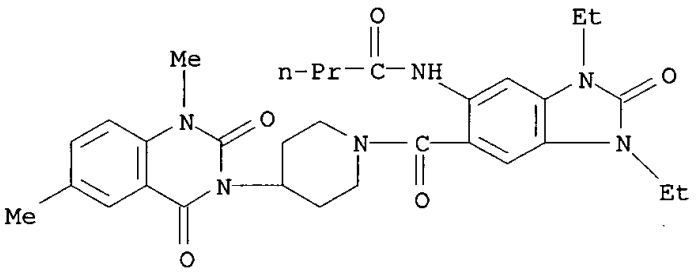
RN 396651-20-0 CAPLUS
CN Acetamide, N-[6-[[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-1,3-diethyl-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl]-2,2,2-trifluoro- (9CI) (CA INDEX NAME)



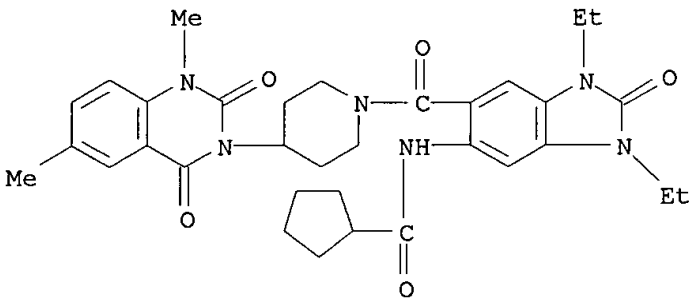
RN 396651-21-1 CAPLUS
CN Propanamide, N-[6-[[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-1,3-diethyl-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl]- (9CI) (CA INDEX NAME)



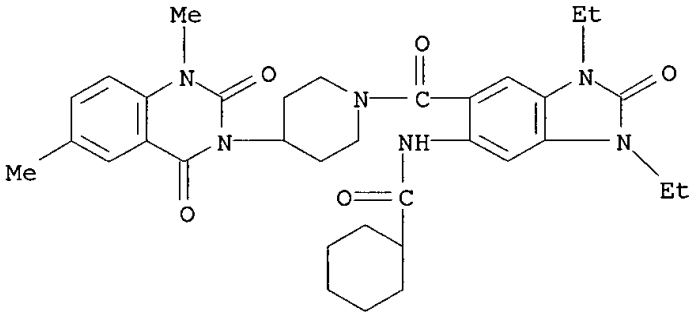
RN 396651-22-2 CAPLUS
CN Butanamide, N-[6-[[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-1,3-diethyl-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl]- (9CI) (CA INDEX NAME)



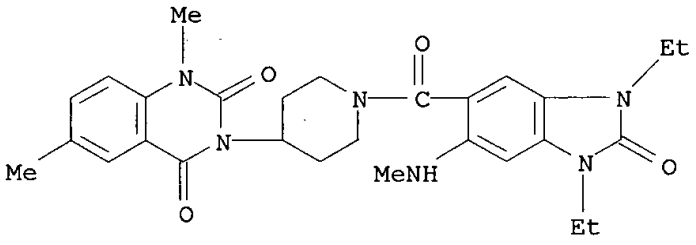
RN 396651-23-3 CAPLUS
CN Cyclopentanecarboxamide, N-[6-[[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-1,3-diethyl-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl]- (9CI) (CA INDEX NAME)



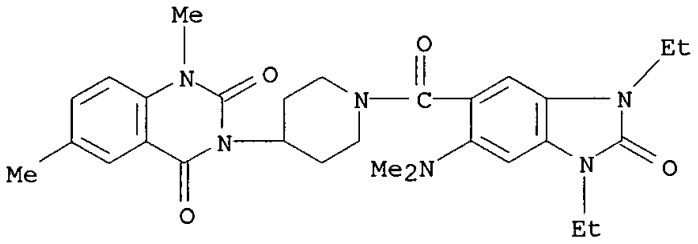
RN 396651-24-4 CAPLUS
CN Cyclohexanecarboxamide, N-[6-[[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-1,3-diethyl-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl]- (9CI) (CA INDEX NAME)



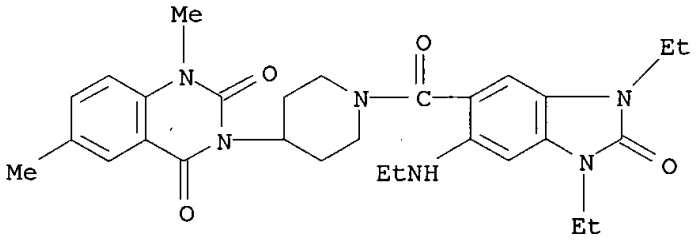
RN 396651-25-5 CAPLUS
CN Piperidine, 1-[[1,3-diethyl-2,3-dihydro-6-(methylamino)-2-oxo-1H-benzimidazol-5-yl]carbonyl]-4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)- (9CI) (CA INDEX NAME)



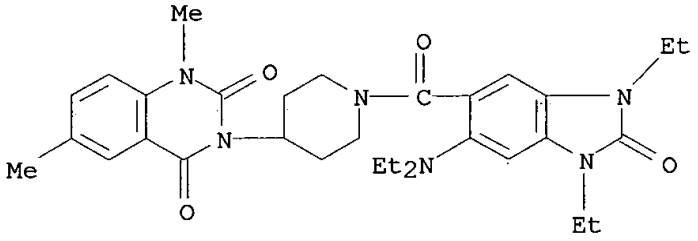
RN 396651-26-6 CAPLUS
CN Piperidine, 4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-[[6-(dimethylamino)-1,3-diethyl-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl]carbonyl]- (9CI) (CA INDEX NAME)



RN 396651-27-7 CAPLUS
CN Piperidine, 1-[[1,3-diethyl-6-(ethylamino)-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl]carbonyl]-4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)- (9CI) (CA INDEX NAME)

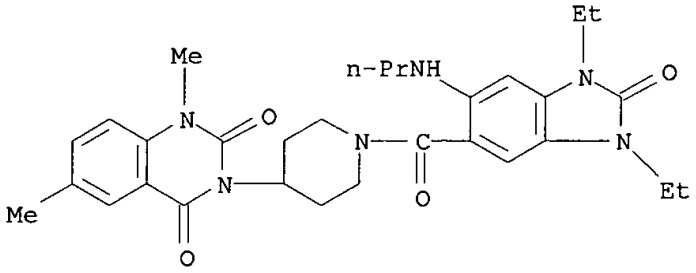


RN 396651-28-8 CAPLUS
CN Piperidine, 1-[[6-(diethylamino)-1,3-diethyl-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl]carbonyl]-4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-, monohydrochloride (9CI) (CA INDEX NAME)



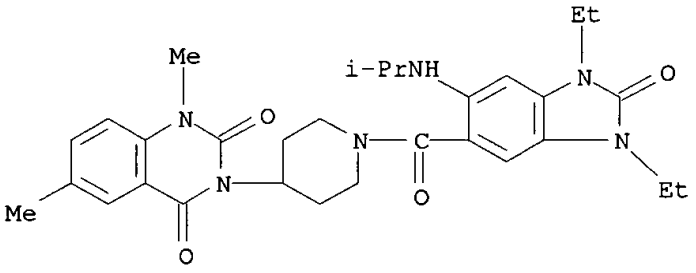
● HCl

RN 396651-29-9 CAPLUS
CN Piperidine, 1-[[1,3-diethyl-2,3-dihydro-2-oxo-6-(propylamino)-1H-benzimidazol-5-yl]carbonyl]-4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-, monohydrochloride (9CI) (CA INDEX NAME)

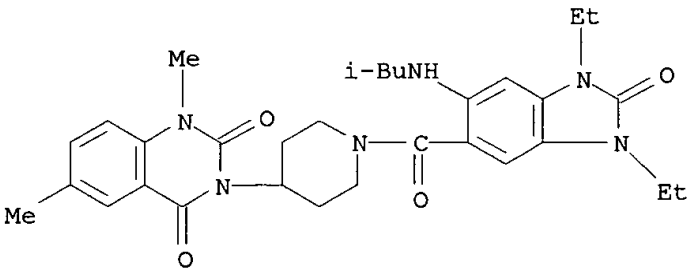


● HCl

RN 396651-30-2 CAPLUS
CN Piperidine, 1-[[1,3-diethyl-2,3-dihydro-6-[(1-methylethyl)amino]-2-oxo-1H-benzimidazol-5-yl]carbonyl]-4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)- (9CI) (CA INDEX NAME)



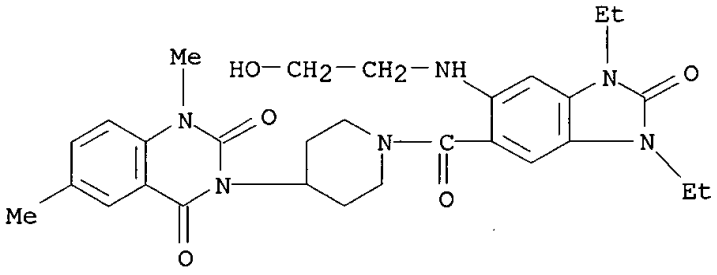
RN 396651-31-3 CAPLUS
CN Piperidine, 1-[[1,3-diethyl-2,3-dihydro-6-[(2-methylpropyl)amino]-2-oxo-1H-benzimidazol-5-yl]carbonyl]-4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-, monohydrochloride (9CI) (CA INDEX NAME)



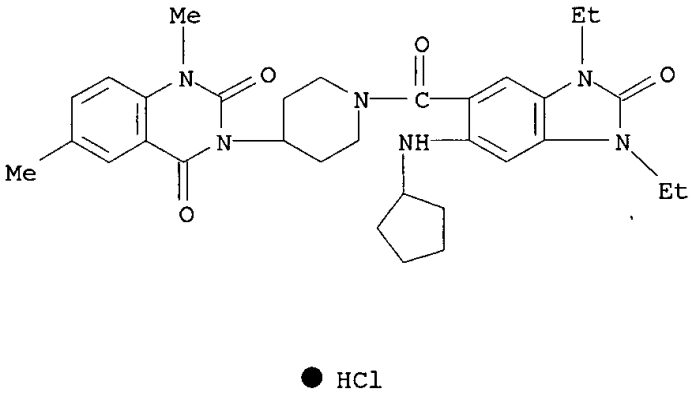
● HCl

RN 396651-32-4 CAPLUS

CN Piperidine, 1-[[1,3-diethyl-2,3-dihydro-6-[(2-hydroxyethyl)amino]-2-oxo-1H-benzimidazol-5-yl]carbonyl]-4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)- (9CI) (CA INDEX NAME)

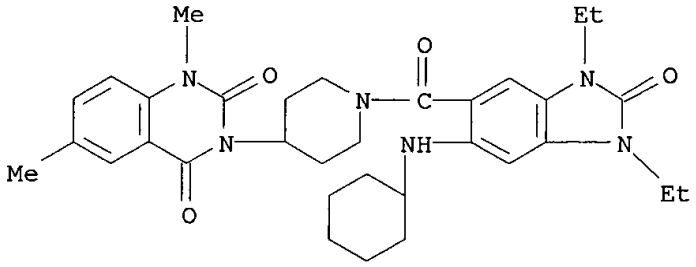


RN 396651-33-5 CAPLUS
CN Piperidine, 1-[[6-(cyclopentylamino)-1,3-diethyl-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl]carbonyl]-4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-, monohydrochloride (9CI) (CA INDEX NAME)



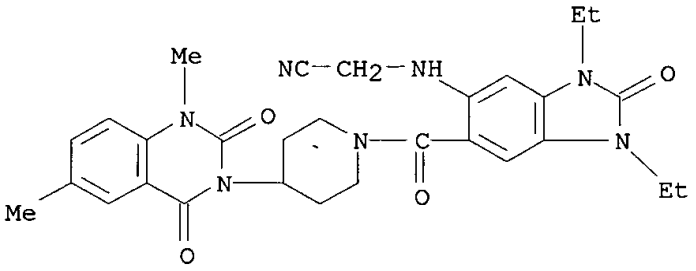
● HCl

RN 396651-34-6 CAPLUS
CN Piperidine, 1-[[6-(cyclohexylamino)-1,3-diethyl-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl]carbonyl]-4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-, monohydrochloride (9CI) (CA INDEX NAME)

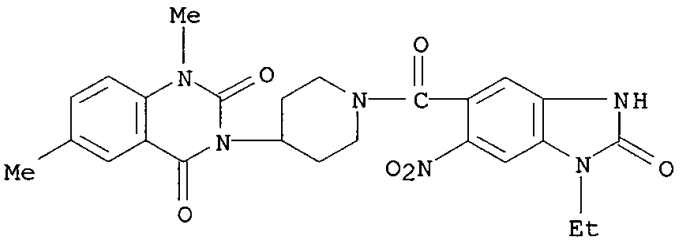


● HCl

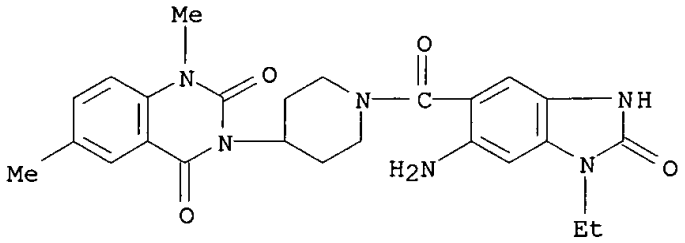
RN 396651-35-7 CAPLUS
CN Piperidine, 1-[[6-[(cyanomethyl)amino]-1,3-diethyl-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl]carbonyl]-4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)- (9CI) (CA INDEX NAME)



RN 396651-36-8 CAPLUS
CN Piperidine, 4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-[(1-ethyl-2,3-dihydro-6-nitro-2-oxo-1H-benzimidazol-5-yl)carbonyl]- (9CI) (CA INDEX NAME)

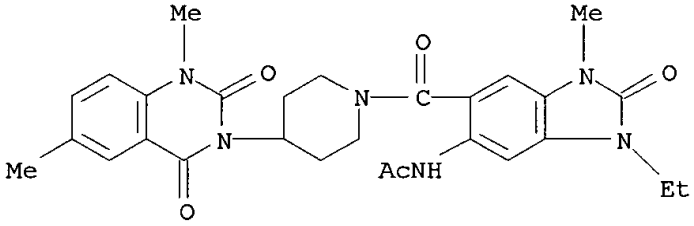


RN 396651-37-9 CAPLUS
CN Piperidine, 1-[(6-amino-1-ethyl-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl)carbonyl]-4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-, monohydrochloride (9CI) (CA INDEX NAME)

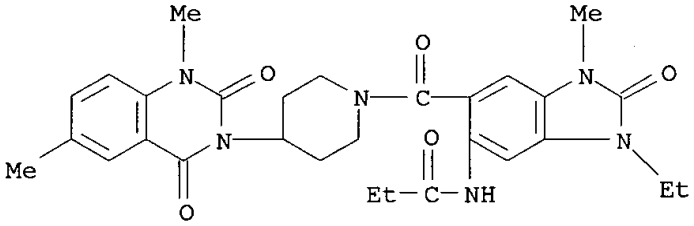


● HCl

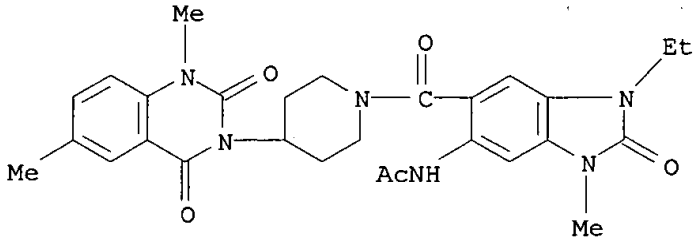
RN 396651-40-4 CAPLUS
CN Acetamide, N-[6-[[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-3-ethyl-2,3-dihydro-1-methyl-2-oxo-1H-benzimidazol-5-yl]- (9CI) (CA INDEX NAME)



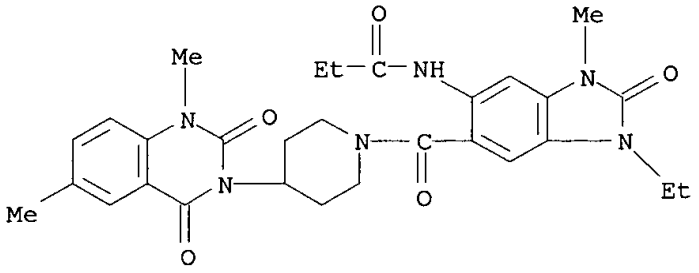
RN 396651-41-5 CAPLUS
CN Propanamide, N-[6-[[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-3-ethyl-2,3-dihydro-1-methyl-2-oxo-1H-benzimidazol-5-yl]- (9CI) (CA INDEX NAME)



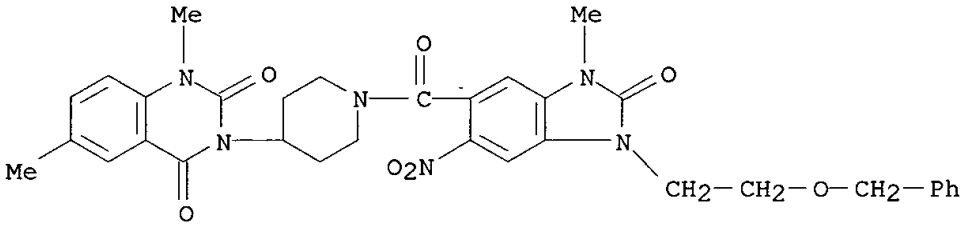
RN 396651-44-8 CAPLUS
CN Acetamide, N-[6-[[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-1-ethyl-2,3-dihydro-3-methyl-2-oxo-1H-benzimidazol-5-yl]- (9CI) (CA INDEX NAME)



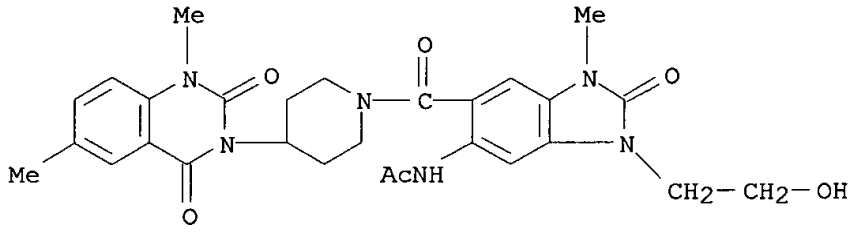
RN 396651-45-9 CAPLUS
CN Propanamide, N-[6-[[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-1-ethyl-2,3-dihydro-3-methyl-2-oxo-1H-benzimidazol-5-yl]- (9CI) (CA INDEX NAME)



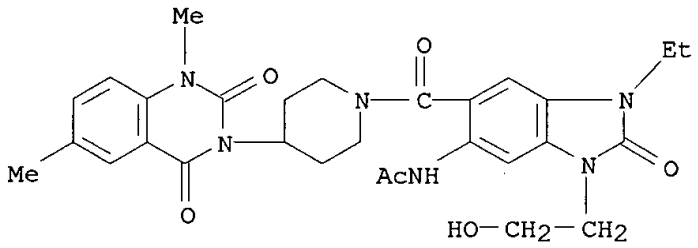
RN 396651-46-0 CAPLUS
CN Piperidine, 4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-[[2,3-dihydro-3-methyl-6-nitro-2-oxo-1-[2-(phenylmethoxy)ethyl]-1H-benzimidazol-5-yl]carbonyl]- (9CI) (CA INDEX NAME)



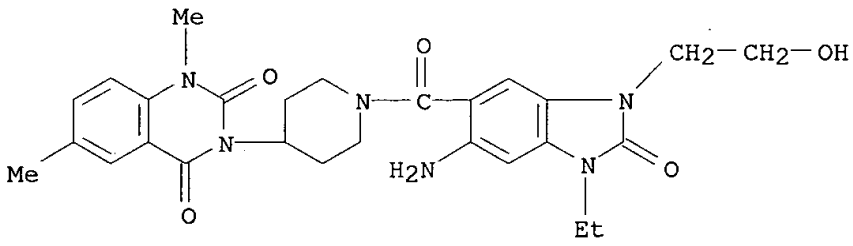
RN 396651-48-2 CAPLUS
CN Acetamide, N-[6-[[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-2,3-dihydro-3-(2-hydroxyethyl)-1-methyl-2-oxo-1H-benzimidazol-5-yl]- (9CI) (CA INDEX NAME)



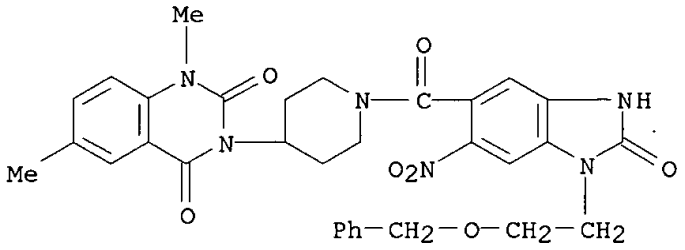
RN 396651-51-7 CAPLUS
CN Acetamide, N-[6-[[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-1-ethyl-2,3-dihydro-3-(2-hydroxyethyl)-2-oxo-1H-benzimidazol-5-yl]- (9CI) (CA INDEX NAME)



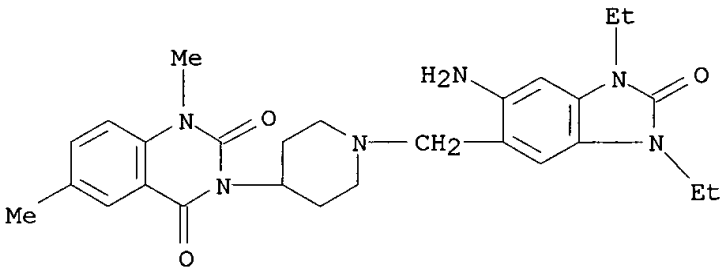
RN 396651-53-9 CAPLUS
CN Piperidine, 1-[[6-amino-1-ethyl-2,3-dihydro-3-(2-hydroxyethyl)-2-oxo-1H-benzimidazol-5-yl]carbonyl]-4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)- (9CI) (CA INDEX NAME)



RN 396651-54-0 CAPLUS
CN Piperidine, 4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-[[2,3-dihydro-6-nitro-2-oxo-1-[2-(phenylmethoxy)ethyl]-1H-benzimidazol-5-yl]carbonyl]- (9CI) (CA INDEX NAME)

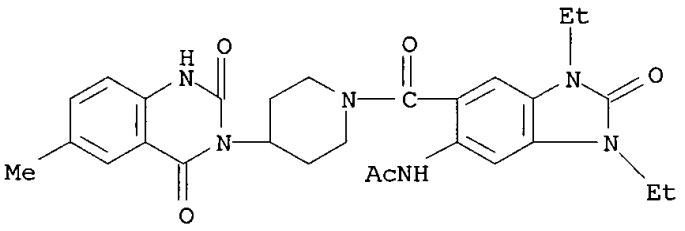


RN 396651-56-2 CAPLUS
CN 2,4(1H,3H)-Quinazolinedione, 3-[1-[(6-amino-1,3-diethyl-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl)methyl]-4-piperidinyl]-1,6-dimethyl-, dihydrochloride (9CI) (CA INDEX NAME)

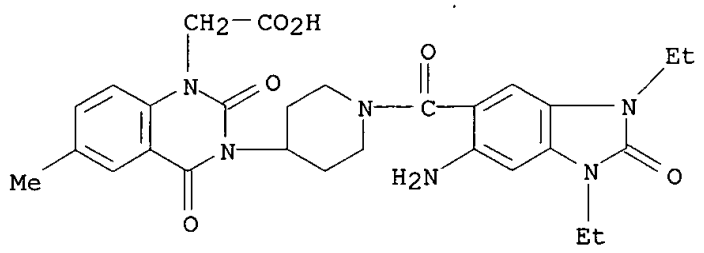


●2 HCl

RN 396651-58-4 CAPLUS
CN Acetamide, N-[6-[[4-(1,4-dihydro-6-methyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-1,3-diethyl-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl]- (9CI) (CA INDEX NAME)

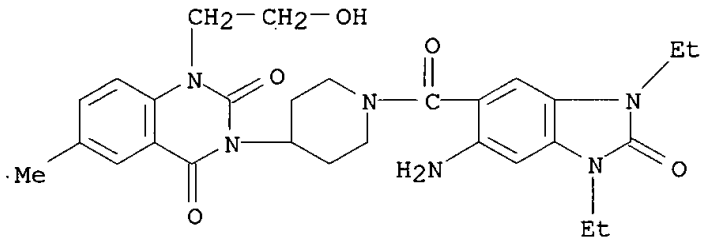


RN 396651-61-9 CAPLUS
CN 1(2H)-Quinazolineacetic acid, 3-[1-[(6-amino-1,3-diethyl-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl)carbonyl]-4-piperidinyl]-3,4-dihydro-6-methyl-2,4-dioxo-, monohydrochloride (9CI) (CA INDEX NAME)

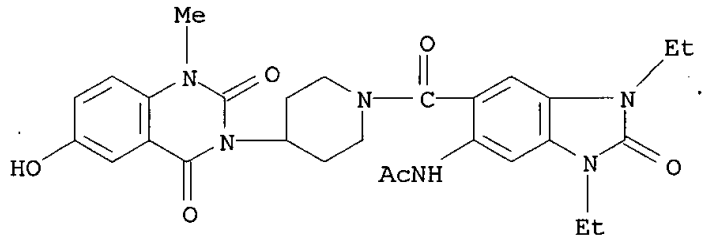


● HCl

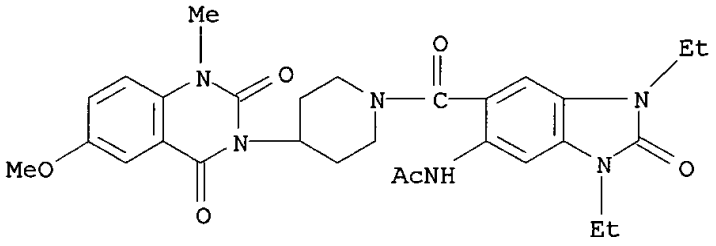
RN 396651-62-0 CAPLUS
CN Piperidine, 1-[(6-amino-1,3-diethyl-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl)carbonyl]-4-[1,4-dihydro-1-(2-hydroxyethyl)-6-methyl-2,4-dioxo-3(2H)-quinazolinyl]- (9CI) (CA INDEX NAME)



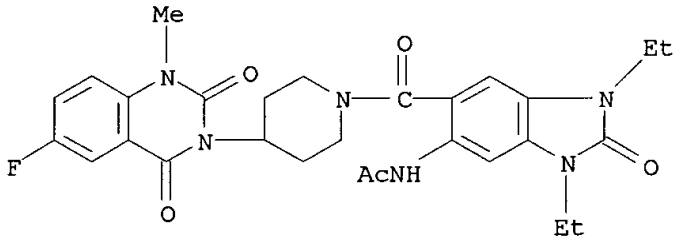
RN 396651-65-3 CAPLUS
CN Acetamide, N-[6-[[4-(1,4-dihydro-6-hydroxy-1-methyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-1,3-diethyl-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl]- (9CI) (CA INDEX NAME)



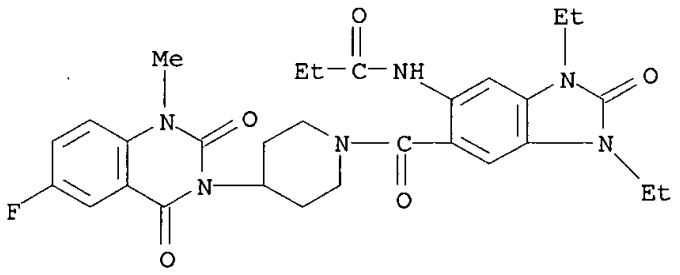
RN 396651-68-6 CAPLUS
CN Acetamide, N-[6-[[4-(1,4-dihydro-6-methoxy-1-methyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-1,3-diethyl-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl]- (9CI) (CA INDEX NAME)



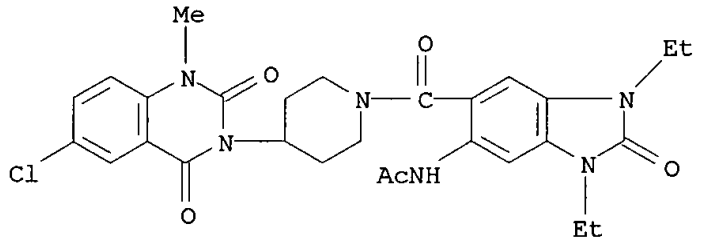
RN 396651-71-1 CAPLUS
CN Acetamide, N-[1,3-diethyl-6-[[4-(6-fluoro-1,4-dihydro-1-methyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl]- (9CI) (CA INDEX NAME)



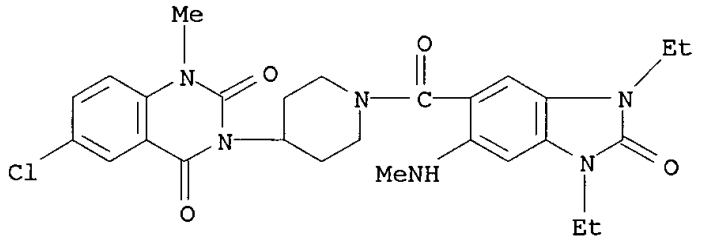
RN 396651-72-2 CAPLUS
CN Propanamide, N-[1,3-diethyl-6-[[4-(6-fluoro-1,4-dihydro-1-methyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl]- (9CI) (CA INDEX NAME)



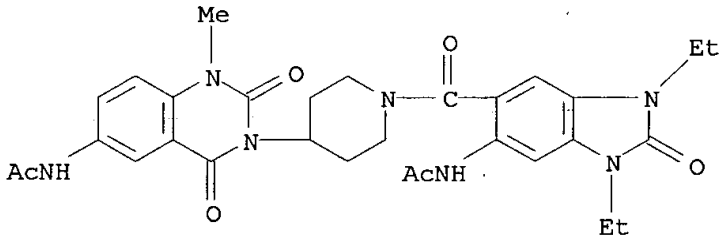
RN 396651-76-6 CAPLUS
CN Acetamide, N-[6-[[4-(6-chloro-1,4-dihydro-1-methyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-1,3-diethyl-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl]- (9CI) (CA INDEX NAME)



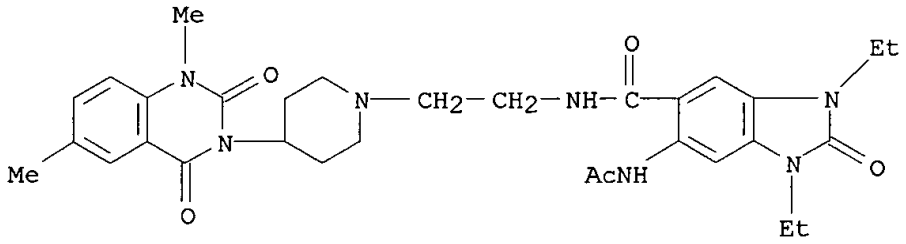
RN 396651-77-7 CAPLUS
CN Piperidine, 4-(6-chloro-1,4-dihydro-1-methyl-2,4-dioxo-3(2H)-quinazolinyl)-1-[[1,3-diethyl-2,3-dihydro-6-(methylamino)-2-oxo-1H-benzimidazol-5-yl]carbonyl]- (9CI) (CA INDEX NAME)



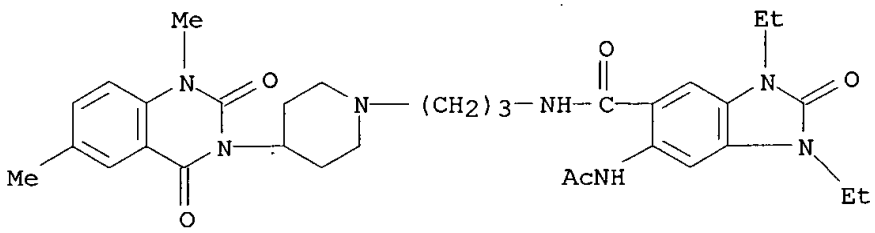
RN 396651-79-9 CAPLUS
CN Acetamide, N-[3-[1-[[6-(acetylamino)-1,3-diethyl-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl]carbonyl]-4-piperidinyl]-1,2,3,4-tetrahydro-1-methyl-2,4-dioxo-6-quinazolinyl]- (9CI) (CA INDEX NAME)



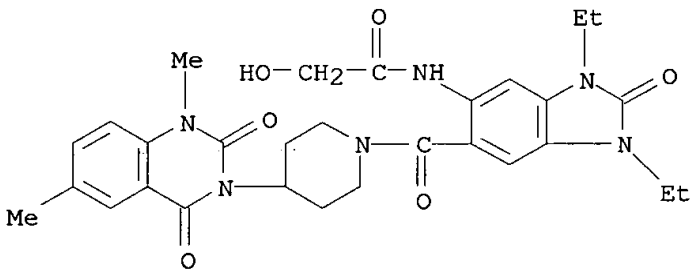
RN 396651-82-4 CAPLUS
CN 1H-Benzimidazole-5-carboxamide, 6-(acetylamino)-N-[2-[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]ethyl]-1,3-diethyl-2,3-dihydro-2-oxo- (9CI) (CA INDEX NAME)



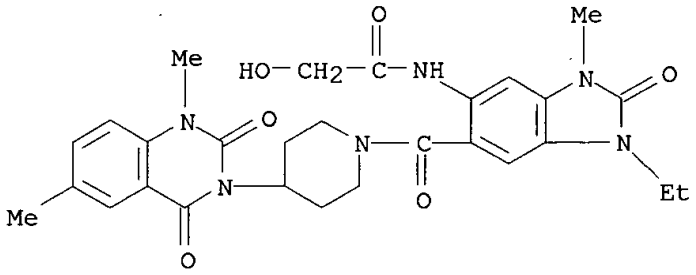
RN 396651-85-7 CAPLUS
CN 1H-Benzimidazole-5-carboxamide, 6-(acetylamino)-N-[3-[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]propyl]-1,3-diethyl-2,3-dihydro-2-oxo- (9CI) (CA INDEX NAME)



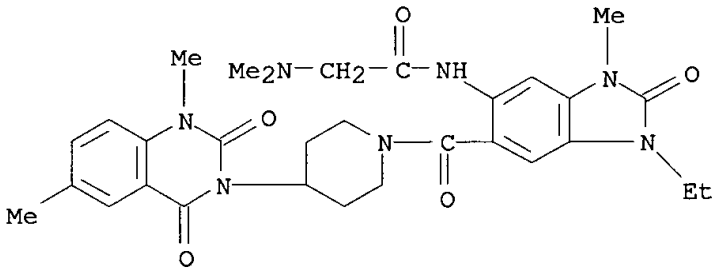
RN 396651-99-3 CAPLUS
CN Acetamide, N-[6-[[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-1,3-diethyl-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl]-2-hydroxy- (9CI) (CA INDEX NAME)



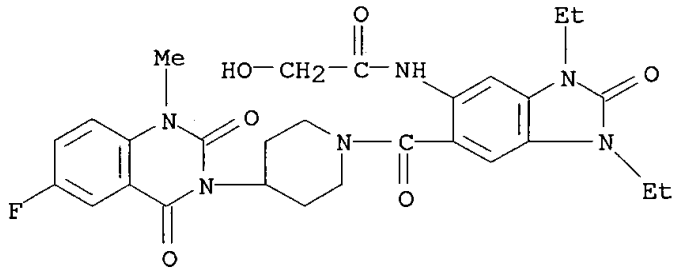
RN 396652-01-0 CAPLUS
CN Acetamide, N-[6-[[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-1-ethyl-2,3-dihydro-3-methyl-2-oxo-1H-benzimidazol-5-yl]-2-hydroxy- (9CI) (CA INDEX NAME)



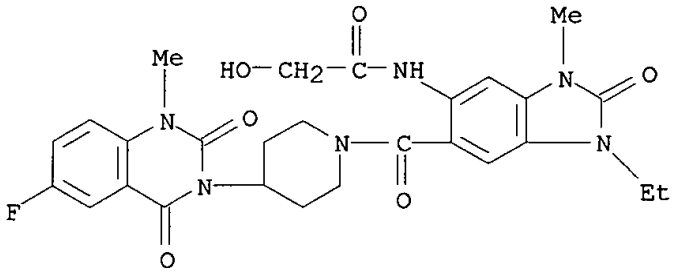
RN 396652-02-1 CAPLUS
CN Acetamide, N-[6-[[4-(1,4-dihydro-1,6-dimethyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-1-ethyl-2,3-dihydro-3-methyl-2-oxo-1H-benzimidazol-5-yl]-2-(dimethylamino)- (9CI) (CA INDEX NAME)



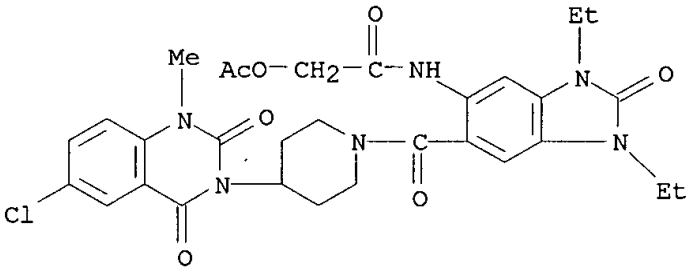
RN 396652-03-2 CAPLUS
CN Acetamide, N-[1,3-diethyl-6-[[4-(6-fluoro-1,4-dihydro-1-methyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl]-2-hydroxy- (9CI) (CA INDEX NAME)



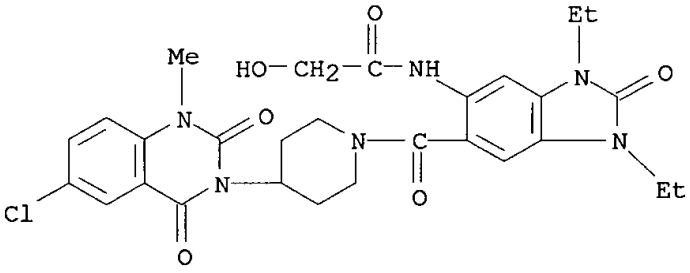
RN 396652-05-4 CAPLUS
CN Acetamide, N-[1-ethyl-6-[[4-(6-fluoro-1,4-dihydro-1-methyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-2,3-dihydro-3-methyl-2-oxo-1H-benzimidazol-5-yl]-2-hydroxy- (9CI) (CA INDEX NAME)



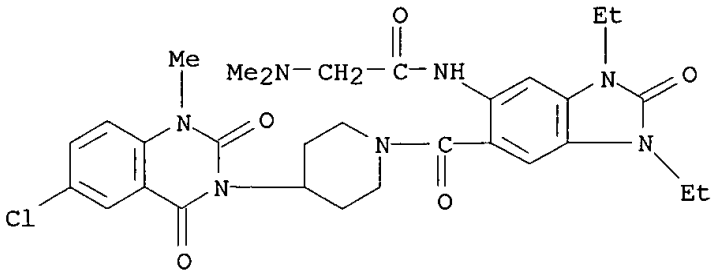
RN 396652-06-5 CAPLUS
CN Acetamide, 2-(acetyloxy)-N-[6-[[4-(6-chloro-1,4-dihydro-1-methyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-1,3-diethyl-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl]- (9CI) (CA INDEX NAME)



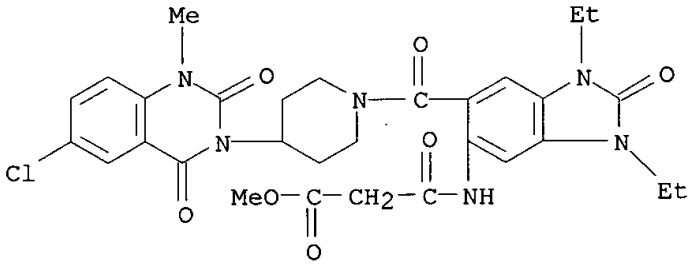
RN 396652-07-6 CAPLUS
CN Acetamide, N-[6-[[4-(6-chloro-1,4-dihydro-1-methyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-1,3-diethyl-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl]-2-hydroxy- (9CI) (CA INDEX NAME)



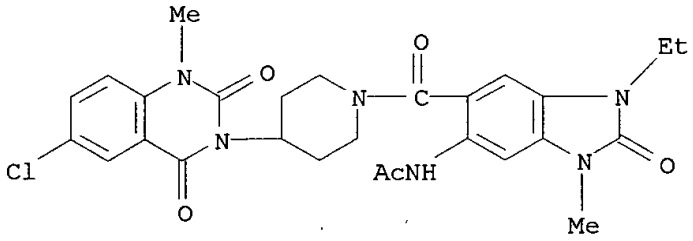
RN 396652-08-7 CAPLUS
CN Acetamide, N-[6-[[4-(6-chloro-1,4-dihydro-1-methyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-1,3-diethyl-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl]-2-(dimethylamino)- (9CI) (CA INDEX NAME)



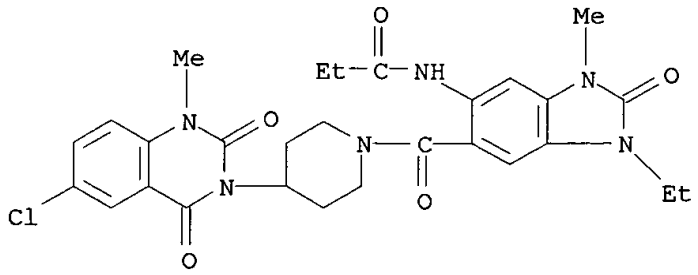
RN 396652-09-8 CAPLUS
CN Propanoic acid, 3-[[6-[[4-(6-chloro-1,4-dihydro-1-methyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-1,3-diethyl-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl]amino]-3-oxo-, methyl ester (9CI) (CA INDEX NAME)



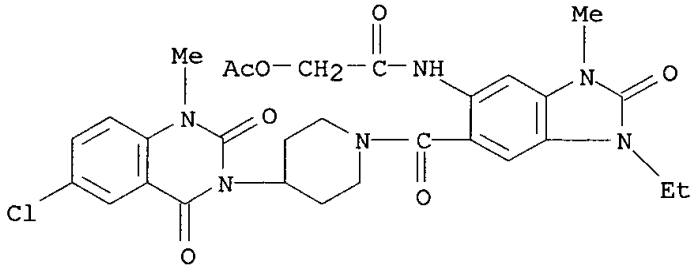
RN 396652-12-3 CAPLUS
CN Acetamide, N-[6-[[4-(6-chloro-1,4-dihydro-1-methyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-1-ethyl-2,3-dihydro-3-methyl-2-oxo-1H-benzimidazol-5-yl]- (9CI) (CA INDEX NAME)



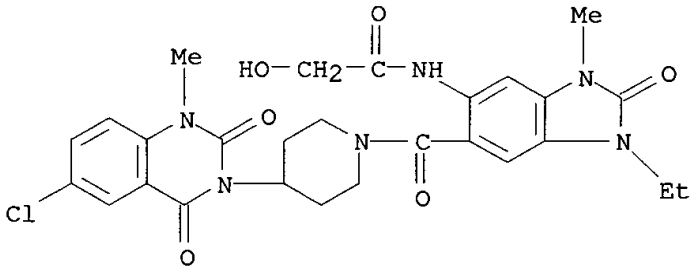
RN 396652-13-4 CAPLUS
CN Propanamide, N-[6-[[4-(6-chloro-1,4-dihydro-1-methyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-1-ethyl-2,3-dihydro-3-methyl-2-oxo-1H-benzimidazol-5-yl]- (9CI) (CA INDEX NAME)



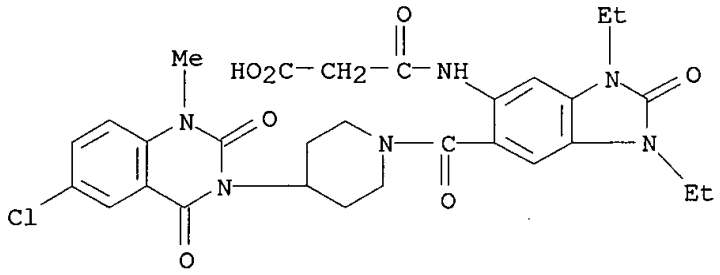
RN 396652-14-5 CAPLUS
CN Acetamide, 2-(acetyloxy)-N-[6-[[4-(6-chloro-1,4-dihydro-1-methyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-1-ethyl-2,3-dihydro-3-methyl-2-oxo-1H-benzimidazol-5-yl]- (9CI) (CA INDEX NAME)



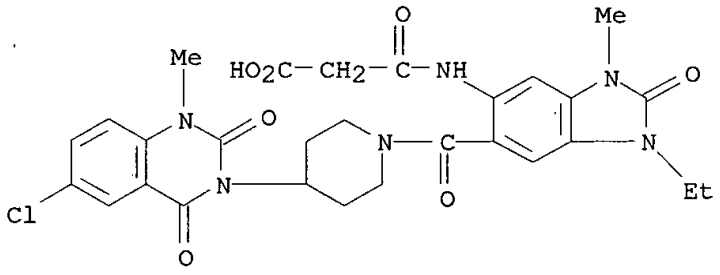
RN 396652-15-6 CAPLUS
CN Acetamide, N-[6-[[4-(6-chloro-1,4-dihydro-1-methyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-1-ethyl-2,3-dihydro-3-methyl-2-oxo-1H-benzimidazol-5-yl]-2-hydroxy- (9CI) (CA INDEX NAME)



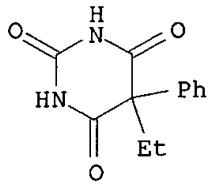
RN 396652-19-0 CAPLUS
CN Propanoic acid, 3-[[6-[[4-(6-chloro-1,4-dihydro-1-methyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-1,3-diethyl-2,3-dihydro-2-oxo-1H-benzimidazol-5-yl]amino]-3-oxo- (9CI) (CA INDEX NAME)



RN 396652-20-3 CAPLUS
CN Propanoic acid, 3-[[6-[[4-(6-chloro-1,4-dihydro-1-methyl-2,4-dioxo-3(2H)-quinazolinyl)-1-piperidinyl]carbonyl]-1-ethyl-2,3-dihydro-3-methyl-2-oxo-1H-benzimidazol-5-yl]amino]-3-oxo- (9CI) (CA INDEX NAME)

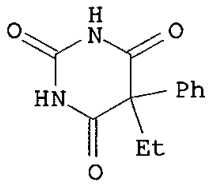


L20 ANSWER 5 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 2002:111814 CAPLUS
DN 136:303543
TI Pharmacokinetics and anticonvulsant effects of diazepam in children with severe falciparum malaria and convulsions
AU Ogutu, B. R.; Newton, C. R. J. C.; Crawley, J.; Muchohi, S. N.; Otieno, G. O.; Edwards, G.; Marsh, K.; Kokwaro, G. O.
CS Kenya Medical Research Institute [KEMRI]/Wellcome Trust Centre for Geographic Medicine Research (Coast), Kilifi, Kenya
SO British Journal of Clinical Pharmacology (2002), 53(1), 49-57
CODEN: BCPHBM; ISSN: 0306-5251
PB Blackwell Science Ltd.
DT Journal
LA English
AB Aims: **Convulsions** are a common complication of severe malaria in children and are assocd. with poor outcome. Diazepam is used to terminate **convulsions** but its pharmacokinetics and pharmacodynamics have not been studied in this group. Accordingly, we carried out a comparative study of the pharmacokinetics of i.v. (i.v.) and rectal (p.r.) diazepam. Methods: Twenty-five children with severe malaria and a **convulsion** lasting > 5 min were studied. Sixteen children received diazepam i.v. (i.v.; 0.3 mg kg-1) and nine rectally (p.r.; 0.5 mg kg-1). Plasma diazepam concns. were measured by reversed phase high-performance liq. chromatog. The duration of **convulsions**, depth of coma, respiratory and cardiovascular parameters were monitored. Results: Median max. plasma diazepam concns. of 634 (range 402-1507) ng ml-1 and 423 (range 112-1953) ng ml-1 were achieved at 5 and 25 min following i.v. and p.r. administration, resp. All patients except three (one i.v. and two p.r.) achieved plasma diazepam concn. >200 ng ml-1 within 5 min. Following p.r. administration, plasma diazepam concns. were more variable than i.v. administration. A single dose of i.v. diazepam terminated **convulsions** in all children but in only 6/9 after p.r. administration. However, nine children **treated** with i.v. and all those **treated** with p.r. diazepam had a recurrence of **convulsions** occurring at median plasma diazepam concns. of 157 (range: 67-169) and 172 (range: 74-393) ng ml-1, resp. All the children in the i.v. and four in the PR diazepam group who had recurrence of **convulsions** required **treatment**. None of the children developed respiratory depression or hypotension. Conclusions: Administration of diazepam i.v. or p.r. resulted in achievement of **therapeutic** concns. of diazepam rapidly, without significant cardio-respiratory adverse effects. However, following p.r. administration, diazepam did not terminate all **convulsions** and plasma drug concns. were more variable.
IT **50-06-6**, Phenobarbitone, biological studies
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(pharmacokinetics and anticonvulsant effects of i.v. and rectal diazepam in children **treated** for severe falciparum malaria and **convulsions**)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)



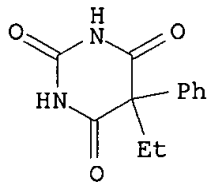
RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 6 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 2001:756402 CAPLUS
DN 136:95941
TI Pharmacologic rescue of lethal seizures in mice deficient in succinate semialdehyde dehydrogenase
AU Hogema, Boris M.; Gupta, Maneesh; Senephansiri, Henry; Burlingame, Terry G.; Taylor, Melissa; Jakobs, Cornelis; Schutgens, Ruud B. H.; Froestl, Wolfgang; Snead, O. Carter; Diaz-Arrastia, Ramon; Bottiglieri, Teodoro; Grompe, Markus; Gibson, K. Michael
CS Department of Molecular and Medical Genetics, Oregon Health Sciences University, Portland, OR, 97201, USA
SO Nature Genetics (2001), 29(2), 212-216
CODEN: NGENEC; ISSN: 1061-4036
PB Nature America Inc.
DT Journal
LA English
AB Succinate semialdehyde dehydrogenase (SSADH, encoded by the gene Aldh5a1) deficiency is a defect of GABA degrdn. that manifests in humans as 4-hydroxybutyric (GHB) aciduria. It is characterized by a nonspecific neurol. disorder including psychomotor retardation, language delay, seizures, hypotonia and ataxia. The current **therapy**, vigabatrin (VGB), is not uniformly successful. This work reports the development of Aldh5a1-deficient mice. At postnatal day 16-22 Aldh5a1-/- mice displayed ataxia and developed generalized seizures leading to rapid death. Increased amts. of GHB and total GABA were found in urine, brain and liver homogenates as well as significant gliosis in the hippocampus of Aldh5a1-/- mice. **Therapeutic** intervention with phenobarbital or phenytoin was ineffective, whereas intervention with VGB or the GABAB receptor antagonist CGP 35348 prevented tonic-clonic **convulsions** and enhanced survival of the mutant mice. Because neurol. deterioration coincided with weaning, the presence of a protective compd. in breast milk was hypothesized. **Treatment** of mutant mice with the amino acid taurine rescued Aldh5a1-/- mice. These findings provide insight into pathomechanisms and may have **therapeutic** relevance for the human SSADH deficiency disease and GHB overdose and toxicity.
IT **50-06-6**, Phenobarbital, biological studies
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(phenobarbital treatment of lethal seizures in gene Aldh5a1-mutant mice deficient in succinate semialdehyde dehydrogenase)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)



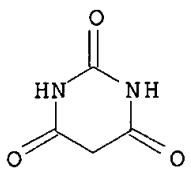
RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 7 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 2001:477963 CAPLUS
DN 136:226629
TI N6-cyclohexyladenosine and 3-(2-carboxypiperazine-4-yl)-1-propenyl-1-phosphonic acid enhance the effect of antiepileptic drugs against induced seizures in mice
AU Assi, Abdel-Azim
CS Dep. Pharmacol., Fac. Med., Assiut Univ., Assiut, Egypt
SO Journal of Pharmacy & Pharmaceutical Sciences [online computer file] (2001), 4(1), 42-51
CODEN: JPPSFY; ISSN: 1482-1826
URL: http://www.ualberta.ca/~csps/JPPS4(1)/A.Assi/epilepsy.pdf
PB Canadian Society for Pharmaceutical Sciences
DT Journal; (online computer file)
LA English
AB Purpose: The influence of N6-Cyclohexyladenosine (CHA), an adenosine A1 agonist and 3-(2-Carboxypiperazine-4-yl)-1-propenyl-1-phosphonic acid (CPPene), a selective N-methyl-D-aspartate (NMDA) antagonist upon the anticonvulsant activity of diazepam (DA), sodium valproate (VP), diphenylhydantoin (DPH), phenobarbital (PB), and carbamazepine (CAZ) was investigated in mice. All agents were administered i.p. Methods: **Convulsive** seizures were induced by the use of electro shocks and pentylenetetrazole (PTZ). Results: CHA (2 mg/kg, i.p.) and CPPene (2.5 mg/kg, i.p.) were found to enhance the anticonvulsant activity of the tested antiepileptic drugs against both electro **convulsions** and PTZ-induced **convulsions**. Both CHA and CPPene significantly decreased the ED50 values of these drugs against both electro **convulsions** and PTZ-induced **convulsions**, and increased the **convulsive** threshold. CHA (2 mg/kg, i.p.) and CPPene (2.5 mg/kg, i.p.) did not affect the plasma level of any of the tested antiepileptic drugs, indicating no pharmacokinetic interactions at the systemic administration. CHA (2 mg/kg, i.p.) or CPPene (2.5 mg/kg, i.p.), alone or in combination with the tested antiepileptic drugs produced no significant changes in their effects on the heart rate, blood pressure, body temp., gross behavior, or on the locomotor activity of exptl. animals. Combinations of the antiepileptic drugs with CHA (2 mg/kg, i.p.) or CPPene (2.5 mg/kg, i.p.) were also devoid of significant effects on the motor performance and long-term memory in mice demonstrated by the Chimney test and passive avoidance task. CHA (5 mg/kg, i.p.) alone or in combination with the tested antiepileptic drugs produced inhibition of locomotor activity and motor coordination, sedation, and hypothermia as well as impairing of long-term memory. Conclusion: Adenosine A1 agonists and NMDA antagonists enhance the efficacy of common antiepileptic drugs, indicating the involvement of adenosine and NMDA receptors in the **convulsive** pathway. The potential **therapeutic** benefits of such interactions may be taken into consideration and merit further investigations in animals and humans.
IT **50-06-6**, Phenobarbital, biological studies
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(N6-cyclohexyladenosine and CPPene enhance effects of antiepileptic drugs)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)



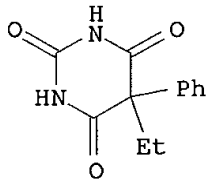
RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 8 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 2001:427618 CAPLUS
DN 135:251301
TI The new generation of GABA enhancers: Potential in the treatment of epilepsy
AU Czuczwar, Stanislaw J.; Patsalos, Philip N.
CS Department of Pathophysiology, Medical University, Lublin, Pol.
SO CNS Drugs (2001), 15(5), 339-350
CODEN: CNDREF; ISSN: 1172-7047
PB Adis International Ltd.
DT Journal; General Review
LA English
AB A review with 76 refs. .gamma.-Aminobutyric acid (GABA) is considered to be the major inhibitory neuro-transmitter in the brain and loss of GABA inhibition has been clearly implicated in epileptogenesis. GABA interacts with 3 types of receptor: GABAA, GABAB and GABAC. The GABAA receptor has provided an excellent target for the development of drugs with an anticonvulsant action. Some clin. useful anti-**convulsants**, such as the benzodiazepines and barbiturates and possibly valproic acid (sodium valproate), act at this receptor. In recent years 4 new anticonvulsants, namely vigabatrin, tiagabine, gabapentin and topiramate, with a mechanism of action considered to be primarily via an effect on GABA, have been licensed. Vigabatrin elevates brain GABA levels by inhibiting the enzyme GABA transaminase which is responsible for intracellular GABA catabolism. In contrast, tiagabine elevates synaptic GABA levels by inhibiting the GABA uptake transporter, GAT1, and preventing the uptake of GABA into neurons and glia. Gabapentin, a cyclic analog of GABA, acts by enhancing GABA synthesis and also by decreasing neuronal calcium influx via a specific subunit of voltage-dependent calcium channels. Topiramate acts, in part, via an action on a novel site of the GABAA receptor. Although these drugs are useful in some patients, overall, they have proven to be disappointing as they have had little impact on the prognosis of patients with intractable epilepsy. Despite this, addnl. GABA enhancing anticonvulsants are presently under development. Ganaxolone, retigabine and pregabalin may prove to have a more advantageous **therapeutic** profile than the presently licensed GABA enhancing drugs. This anticipation is based on 2 characteristics. First, they act by hitherto unique mechanisms of action in enhancing GABA-induced neuronal inhibition. Secondly, they act on addnl. antiepileptogenic mechanisms. Finally, CGP 36742, a GABAB receptor antagonist, may prove to be particularly useful in the management of primary generalized absence seizures. The exact impact of these new GABA-enhancing drugs in the **treatment** of epilepsy will have to await their licensing and a period of postmarketing surveillance. As to clarification of their role in the management of epilepsy, this will have to await further clin. trials, particularly direct comparative trials with other anticonvulsants.
IT **67-52-7**, 2,4,6(1H,3H,5H)-Pyrimidinetrione
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(derivs., barbiturates; treatment of epilepsy with new generation of GABA enhancers)
RN 67-52-7 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione (9CI) (CA INDEX NAME)



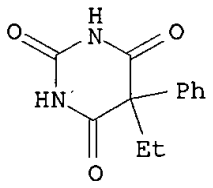
RE.CNT 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 9 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 2001:315398 CAPLUS
DN 135:190297
TI Amlodipine enhances the activity of antiepileptic drugs against pentylenetetrazole-induced seizures
AU Kaminski, R. M.; Mazurek, M.; Turski, W. A.; Kleinrok, Z.; Czuczwar, S. J.
CS Isotope Laboratory, Institute of Agricultural Medicine, Lublin, Pol.
SO Pharmacology, Biochemistry and Behavior (2001), 68(4), 661-668
CODEN: PBBHAU; ISSN: 0091-3057
PB Elsevier Science Inc.
DT Journal
LA English
AB Amlodipine (AML), which belongs to the 1,4-dihydropyridine calcium channel antagonists, possesses pharmacol. and pharmacokinetic profile that distinguishes it from other agents of this class. Pentylenetetrazole (PTZ)-induced clonic and tonic **convulsions** in mice were significantly reduced by administration of AML at 10 mg/kg. At this dose AML remained without influence upon the plasma level of PTZ. The ED50 value of AML against clonic seizures induced by PTZ was 5.4 mg/kg. This calcium channel antagonist (at 2.5 mg/kg) combined with ethosuximide (ETX), valproate magnesium (VPA) or phenobarbital (PB) significantly reduced their ED50 values against clonic phase of PTZ-induced seizures. AML administered alone or in combination with antiepileptic drugs (AEDs) worsened the motor performance of mice in the chimney test. However, these **treatments** remained without significant influence on the retention time in the passive avoidance test. Plasma levels of antiepileptics remained unchanged in the presence of AML. The results indicate that AML does not seem a good candidate for a combination **therapy** in epileptic patients because of its adverse potential.
IT **50-06-6**, Phenobarbital, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(amlodipine enhances the activity of antiepileptic drugs against pentylenetetrazole-induced seizures)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)

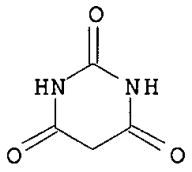


RE.CNT 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

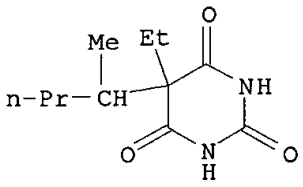
L20 ANSWER 10 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 2001:81972 CAPLUS
DN 135:102413
TI Evaluation of motor toxicity and anticonvulsant efficacy of barbiturates and benzodiazepines in a bicyclophosphate seizure model in mice
AU Liu, Wu-Fu; Chen, Gou-Wei; Wu, Tseng-Rong
CS Laboratory of Behavioral Pharmacology and Toxicology Chemical Systems Research Division, CSIST, Lungtan, 32526, Taiwan
SO Neurotoxicity Research (2000), 2(4), 311-320
CODEN: NURRFI; ISSN: 1029-8428
PB Harwood Academic Publishers
DT Journal
LA English
AB 1. 4-Alkyl derivs. of 2,6,7-trioxa-1-phosphabicyclo[2.2.2]octane-I-oxide [Bicyclophosphates (BP)] are highly toxic **convulsants** and potent GABAA receptor antagonists. 2. The effects of various clin. used anticonvulsant drugs, barbiturates and benzodiazepines, on motor performance and 4-isopropylbicyclophosphate (IPBP), a homolog of BP, induced myoclonic and generalized tonic-clonic seizures were investigated in mice. 3. The anticonvulsant drugs were IP administered 30 min. prior to the inverted screen test, a measure of minimal neurol. deficit, and were then challenged with a 97% **convulsant** dose of IPBP (0.15 mg/kg, SC). 4. The results show that: (1) benzodiazepines are more likely to have favorable motor toxicity and anticonvulsant profiles than barbiturates. (2) Various doses of these drugs that did not significantly cause motor impairment increase the mean latencies to myoclonic and generalized tonic-clonic seizures. (3) The increase in anticonvulsant activity is assocd. with a comparable increase in motor impairment. (4) Only 45-0088-S, an open-ring deriv. of 1,4-benzodiazepines, and clonazepam have protective indexes of more than 5, a satisfactory margin of safety. 5. The potential use of 45-0088-S and clonazepam in the **treatment** of BP-induced seizures should be explored further.
IT **50-06-6**, Phenobarbital, biological studies **67-52-7D**, 2,4,6(1H,3H,5H)-Pyrimidinetrione, derivs. **76-74-4**, Pentobarbital
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(evaluation of motor toxicity and anticonvulsant efficacy of barbiturates and benzodiazepines in a bicyclophosphate seizure model in mice)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)



RN 67-52-7 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione (9CI) (CA INDEX NAME)

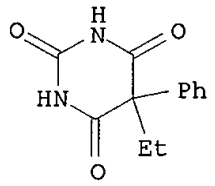


RN 76-74-4 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-(1-methylbutyl)- (9CI) (CA INDEX NAME)



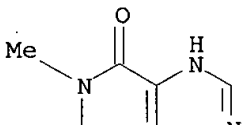
RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 11 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 2000:640976 CAPLUS
DN 134:110348
TI Protection by conventional and new antiepileptic drugs against lindane-induced seizures and lethal effects in mice
AU Tochman, Anna M.; Kaminski, Refal; Turski, Waldemar A.; Czuczwar, Stanislaw J.
CS Isotope Laboratory, Institute of Agricultural Medicine, Lublin, 20-090, Pol.
SO Neurotoxicity Research (2000), 2(1), 63-70
CODEN: NURRFI; ISSN: 1029-8428
PB Harwood Academic Publishers
DT Journal
LA English
AB Toxic effects caused by the organochlorine xenobiotic lindane may result from too excessive antiscabicidal **treatment** and in cases of accidental or intentional poisoning. Predominant symptoms of lindane intoxication concern the central nervous system, e.g. different manifestation of hyperexcitability and epileptiform activity. The inhibition of GABA-ergic neurotransmission seems to be responsible for the **convulsant** activity of lindane. This study was intended to compare the protective activity of conventional and new antiepileptic drugs against **convulsions** and lethal effects elicited by lindane administration in mice. Diazepam, clonazepam, and phenobarbital protected against full seizure pattern and lethal effects evoked by lindane. Carbamazepine, phenytoin, gabapentin, felbamate, and lamotrigine inhibited only lindane-induced tonic **convulsions** and mortality. It may be concluded that apart from benzodiazepines, phenobarbital and, to a lesser extent, carbamazepine, phenytoin, gabapentin, felbamate, and lamotrigine could be used in lindane poisoning. Vigabatrin proved completely ineffective against seizures or lethal effects elicited by lindane.
IT **50-06-6**, Phenobarbital, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(antiepileptic drugs against lindane-induced seizures and lethal effects)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)



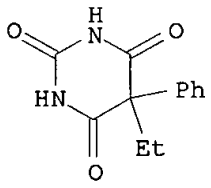
RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 12 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 2000:480995 CAPLUS
DN 133:317414
TI Acute and subacute toxicities of theophylline are directly reflected by its plasma concentration in dogs
AU Shibata, M.; Wachi, M.; Kagawa, M.; Kojima, J.; Onodera, K.
CS Toxicology Group, Nikken Chemicals Co., Ltd., Saitama, Japan
SO Methods and Findings in Experimental and Clinical Pharmacology (2000), 22(3), 173-178
CODEN: MFEPDX; ISSN: 0379-0355
PB Prous Science
DT Journal
LA English
AB The purpose of this study was to evaluate the relationship between acute and subacute toxicity and blood levels of theophylline in dogs. Theophylline was administered i.v. into dogs once (at doses of 50, 100 and 150 mg/kg) or for 4 wk (at doses of 20, 35 and 70 mg/kg/day). In the single dose toxicity study, by increasing the dose of theophylline, plasma concn. increased and the severity of toxic symptoms were intensified. After a single dosing of theophylline, accentuated heart rate and vomiting were obsd. at a concn. of more than 67 .mu.g/mL, and excitement, spasm and hyperpnea were obsd. at more than 130 .mu.g/mL. Animals died after tonic **convulsion** at 180 .mu.g/mL. In the repeated dose toxicity study, the plasma concn. of theophylline increased dependent on dosage, and was not affected by repeated dosing. Even under these conditions, the toxic symptoms were quite similar to those of the single dose, except for an addnl. decrease in movement, body wt. redn. and myocardial lesion. These present results suggest that the severity of theophylline toxicity is dependent on its plasma concns. rather than accumulated dosages. The blood concn. of theophylline-**treated** patients should be maintained within the **therapeutic** range in order to diminish risk.
IT **58-55-9**, Theophylline, biological studies
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(acute and subacute toxicities of theophylline are directly reflected by its plasma concn. in dogs)
RN 58-55-9 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)



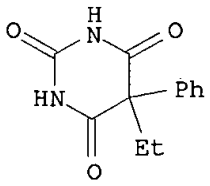
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 13 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 2000:434968 CAPLUS
DN 133:172032
TI Interaction of topiramate with conventional antiepileptic drugs in mice
AU Swiader, M.; Kotowski, J.; Gasior, M.; Kleinrok, Z.; Czuczwar, S. J.
CS Department of Pharmacology and Toxicology, Medical University, Lublin, Pol.
SO European Journal of Pharmacology (2000), 399(1), 35-41
CODEN: EJPHAZ; ISSN: 0014-2999
PB Elsevier Science B.V.
DT Journal
LA English
AB Topiramate [2,3:4,5-bis-O-(1-methyl-ethylidene-)-.beta.-d-fructopyranose sulfamate], administered i.p. up to 5 mg/kg, did not influence the threshold for electroconvulsions. In doses of 10-30 mg/kg, topiramate significantly raised the threshold. This novel antiepileptic drug, in subprotective doses, enhanced the protective activity of i.p. given valproate, carbamazepine, diphenylhydantoin and phenobarbital against maximal electroshock-induced **convulsions** in mice. The potentiation induced by topiramate (2.5-5 mg/kg) was most profound for carbamazepine and phenobarbital. The anticonvulsive activity of valproate and diphenylhydantoin was potentiated by topiramate only at 5 mg/kg. Topiramate (5 mg/kg) combined with valproate, phenobarbital and diphenylhydantoin did not alter their free plasma levels but its combination with carbamazepine resulted in an increased free plasma level of this antiepileptic drug. **Treatment** with topiramate (5 mg/kg) alone or in combination with the studied antiepileptics (providing 50% protection against maximal electroshock) resulted in no adverse effects, as measured in the chimney test (motor coordination) or passive avoidance task (long-term memory). In contrast, valproate administered alone at its ED50 against maximal electroshock impaired motor coordination. It is noteworthy that valproate and carbamazepine at their resp. ED50 values of 248 and 11.2 mg/kg disturbed long-term memory. The results provide an exptl. basis for rational polytherapy.
IT **50-06-6**, Phenobarbital, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(interaction of topiramate with conventional antiepileptic drugs in mice)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)



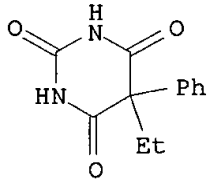
RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 14 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 2000:189579 CAPLUS
DN 132:343184
TI Phenobarbital administration directed against kindled seizures delays functional recovery following brain insult
AU Montanez, S.; Kline, A. E.; Gasser, T. A.; Hernandez, T. D.
CS Campus Box 345, Department of Psychology, Behavioral Neuroscience Program, The University of Colorado, Boulder, CO, USA
SO Brain Research (2000), 860(1,2), 29-40
CODEN: BRREAP; ISSN: 0006-8993
PB Elsevier Science B.V.
DT Journal
LA English
AB Anti-**convulsant** drug administration or recurrent seizures can impact functional recovery following brain insult. The nature of that impact depends on a variety of factors, including timing of drug administration and drug mechanism of action, as well as seizure no., timing, and severity. The objective of this study was to det. the functional consequences of anti-**convulsant** administration directed against seizure activity in brain-damaged animals. To this end, phenobarbital was coupled with daily elec. kindling of the amygdala beginning 48 h after a unilateral anteromedial cortex lesion. Recovery from somatosensory deficits was assessed, as was regional atrophy and basic fibroblast growth factor (bFGF) expression. Animals receiving phenobarbital prior to daily kindling failed to recover within 2 mo of testing. In contrast, animals receiving saline prior to kindling as well as phenobarbital-**treated** non-kindled animals recovered within 2 mo after the lesion. Though the exact mechanisms underlying these behavioral phenomena remain uncertain, patterns of bFGF expression among the groups provide some insight. Taken together, results from the present study suggest that anti-**convulsant** drug administration directed against subclin. seizure activity can be more detrimental to functional recovery than seizures alone or anti-**convulsant** drug **treatment** after seizure activity has occurred.
IT **50-06-6**, Phenobarbital, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(phenobarbital administration directed against kindled seizures delays functional recovery following brain insult)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)



RE.CNT 94 THERE ARE 94 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 15 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 2000:142137 CAPLUS
DN 132:303372
TI Sodium valproate inhibits production of TNF-.alpha. and IL-6 and activation of NF-.kappa.B
AU Ichiyama, T.; Okada, K.; Lipton, J. M.; Matsubara, T.; Hayashi, T.; Furukawa, S.
CS Department of Pediatrics, Yamaguchi University School of Medicine, Ube, Japan
SO Brain Research (2000), 857(1,2), 246-251
CODEN: BRREAP; ISSN: 0006-8993
PB Elsevier Science B.V.
DT Journal
LA English
AB Sodium valproate (VPA) is frequently used to **treat** epilepsy and **convulsive** disorders. Several reports have indicated that anti-epileptic drugs (AED) affect the immune system, but the mechanism has not been clear. We examd. whether the commonly used AEDs, diazepam (DZP), carbamazepine (CBZ), phenobarbital (PB), phenytoin (PHT), and VPA, can inhibit activation of the nuclear transcription factor kappa B (NF-.kappa.B), in human monocytic leukemia cells (THP-1) and in human glioma cells (A-172). NF-.kappa.B is essential to the expression of the kappa light chain of Ig and proinflammatory cytokines. Electrophoretic mobility shift assays (EMSA) of nuclear exts. demonstrated that VPA inhibits NF-.kappa.B activation induced by lipopolysaccharide (LPS), but the other AEDs do not. Western blot anal. revealed that this inhibition is not linked to preservation of expression of I.kappa.B.alpha. protein. Chloramphenicol acetyltransferase (CAT) assay indicated that NF-.kappa.B-dependent reporter gene expression is suppressed in glioma cells pretreated with VPA. VPA significantly inhibited LPS-induced prodn. of TNF-.alpha. and IL-6 by THP-1 cells, whereas other AEDs did not. The findings are consistent with the idea that VPA suppresses TNF-.alpha. and IL-6 prodn. via inhibition of NF-.kappa.B activation. Our results suggest that VPA can modulate immune responses in vitro. These findings raise the possibility that such modulation might occur with clin. use of VPA.
IT **50-06-6**, Phenobarbital, biological studies
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(sodium valproate inhibits prodn. of TNF-.alpha. and IL-6 and activation of NF-.kappa.B)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)



RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 16 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 2000:60825 CAPLUS
DN 132:246248
TI Lethal seizures predicted after aminophylline therapy in cocaine abusers
AU Gasior, M.; Ungard, J. T.; Witkin, J. M.
CS Behavioral Neuroscience Research Branch, Drug Development Group, National Institute on Drug Abuse, NIH, Baltimore, MD, USA
SO European Journal of Pharmacology (2000), 387(2), R15-R16
CODEN: EJPHAZ; ISSN: 0014-2999
PB Elsevier Science B.V.
DT Journal
LA English
AB Mice with a history of chronic (10 days), but not acute, **treatment** with a non-**convulsant** dose of cocaine showed increased sensitivity ($P<0.001$) to the toxic effects of aminophylline (seizures, lethality) relative to controls even days after the cessation of cocaine **treatment**. The present finding suggests that individuals with a history of cocaine use may be at increased risk for **convulsive** and lethal complications assocd. with the **therapeutic** use of aminophylline.
IT **317-34-0**, Aminophylline
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(lethal seizures predicted after aminophylline therapy in cocaine abusers)
RN 317-34-0 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-, compd. with 1,2-ethanediamine (2:1) (9CI) (CA INDEX NAME)

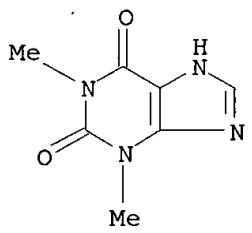
CM 1

CRN 107-15-3
CMF C2 H8 N2

$H_2N-CH_2-CH_2-NH_2$

CM 2

CRN 58-55-9
CMF C7 H8 N4 O2



RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 17 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 2000:34961 CAPLUS
DN 132:73661
TI Cells and animals deficient in the .epsilon. isoenzyme of protein kinase C and their use in screening for anxiolytics
IN Messing, Robert O.; Hodge, Clyde W.
PA USA
SO PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

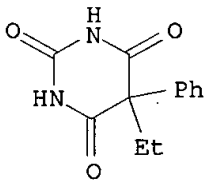
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000001805	A1	20000113	WO 1999-US15152	19990702
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2002124272	A1	20020905	US 1999-340283	19990625
	AU 9949689	A1	20000124	AU 1999-49689	19990702
	EP 1095136	A1	20010502	EP 1999-933688	19990702
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002522012	T2	20020723	JP 2000-558195	19990702
	ZA 2000007494	A	20020415	ZA 2000-7494	20001214
	ZA 2000007780	A	20020322	ZA 2000-7780	20001221
	US 2002151465	A1	20021017	US 2002-39278	20020104
PRAI	US 1998-91755P	P	19980706		
	US 1999-125995P	P	19990324		
	US 1999-340283	A	19990625		
	US 1998-91755	P	19980706		
	US 1998-103763P	P	19981009		
	US 1999-125995	P	19990324		
	WO 1999-US15152	W	19990702		
	US 1999-347370	A1	19990706		

AB Cells and animals deficient in protein kinase C .epsilon. isoenzyme (PKC.epsilon.) that can be used to screen for anti-anxiety drugs are described. According to the present invention, PKC.epsilon.-inhibiting compds. act in synergy with drugs acting at the GABAA receptor. These modulators of PKC.epsilon. may also be used to modulate alc. consumption, self-administration of other drugs of abuse, and the effects of alc. consumption. PKC.epsilon. inhibitors may also also be used either alone or in conjunction with allosteric agonists of GABAA receptors, to **treat** conditions, such as addiction, withdrawal syndrome, skeletal muscle spasms, **convulsive** seizures, and epilepsy, that are amenable to **treatment** by allosteric agonists of GABAA receptors. Addnl. aspects of the present invention are diagnostic methods for identifying individuals at risk for becoming alcoholics or abusers of other drugs and kits for performing such diagnostic methods. Transgenic homozygous PKC.epsilon. knockout mice were found to show lower levels of anxiety than control animals. Gross anatomy of the knockout mice is essentially normal, but there are changes in the patterns of fiber

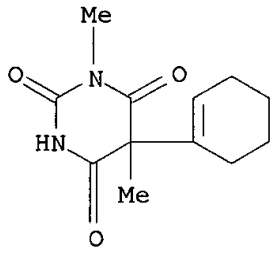
outgrowth and branching in the stratum radiatum. The knockout mice showed lower levels of alc. consumption in ethanol preference drinking tests with a 75% lowering of ethanol preference but did no show any altered preference for sweet (saccharin) or bitter (quinine) flavors or change in general caloric intake. These mice were also hypersensitive to the sedating effects of alc. and to the allosteric GABAA agonists pentobarbital and diazepam.

IT **50-06-6D**, Phenobarbital, mixts. with protein kinase C.epsilon. inhibitors **50-09-9D**, Hexobarbital sodium, mixts. with protein kinase C.epsilon. inhibitors **50-11-3D**, Metharbital, mixts. with protein kinase C.epsilon. inhibitors **57-30-7D**, Phenobarbital sodium, mixts. with protein kinase C.epsilon. inhibitors **57-33-0D**, Pentobarbital sodium, mixts. with protein kinase C.epsilon. inhibitors **57-43-2D**, Amobarbital, mixts. with protein kinase C.epsilon. inhibitors **64-43-7D**, Amobarbital sodium, mixts. with protein kinase C.epsilon. inhibitors **67-52-7D**, 2,4,6(1H,3H,5H)-Pyrimidinetrione, derivs., mixts. with protein kinase C.epsilon. inhibitors **76-73-3D**, Secobarbital, mixts. with protein kinase C.epsilon. inhibitors **76-74-4D**, Pentobarbital, mixts. with protein kinase C.epsilon. inhibitors **77-02-1D**, Aprobarbital, mixts. with protein kinase C.epsilon. inhibitors **115-38-8D**, Mephobarbital, mixts. with protein kinase C.epsilon. inhibitors **115-44-6D**, Talbutal, mixts. with protein kinase C.epsilon. inhibitors **143-81-7D**, Butabarbital sodium, mixts. with protein kinase C.epsilon. inhibitors **309-36-4D**, Methohexital sodium, mixts. with protein kinase C.epsilon. inhibitors **309-43-3D**, Secobarbital sodium, mixts. with protein kinase C.epsilon. inhibitors
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(as anxiolytics or in treatment of drug abuse; cells and animals deficient in .epsilon. isoenzyme of protein kinase C and their use in screening for anxiolytics)

RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)

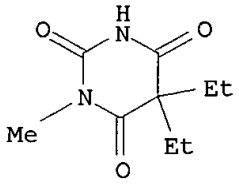


RN 50-09-9 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-(1-cyclohexen-1-yl)-1,5-dimethyl-, sodium salt (9CI) (CA INDEX NAME)

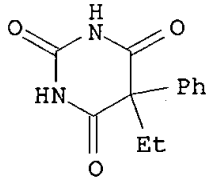


● Na

RN 50-11-3 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5,5-diethyl-1-methyl- (9CI) (CA INDEX NAME)

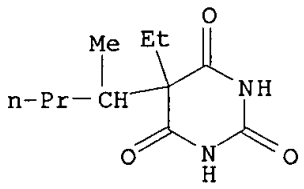


RN 57-30-7 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl-, monosodium salt (9CI) (CA INDEX NAME)



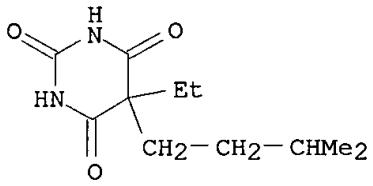
● Na

RN 57-33-0 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-(1-methylbutyl)-, monosodium salt (9CI) (CA INDEX NAME)

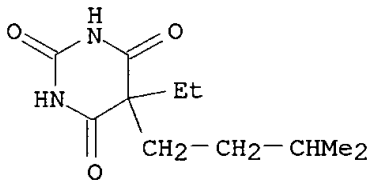


● Na

RN 57-43-2 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-(3-methylbutyl)- (9CI) (CA INDEX NAME)

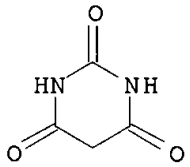


RN 64-43-7 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-(3-methylbutyl)-, monosodium salt (9CI) (CA INDEX NAME)

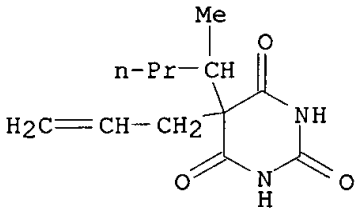


● Na

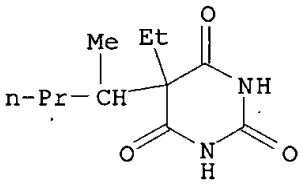
RN 67-52-7 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione (9CI) (CA INDEX NAME)



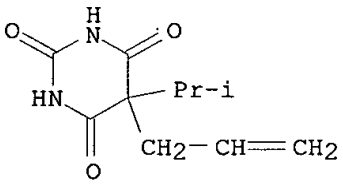
RN 76-73-3 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-(1-methylbutyl)-5-(2-propenyl)- (9CI) (CA INDEX NAME)



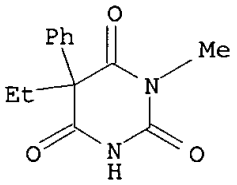
RN 76-74-4 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-(1-methylbutyl)- (9CI) (CA INDEX NAME)



RN 77-02-1 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-(1-methylethyl)-5-(2-propenyl)- (9CI) (CA INDEX NAME)

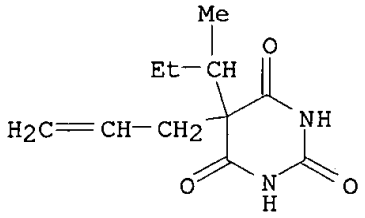


RN 115-38-8 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-1-methyl-5-phenyl- (9CI) (CA INDEX NAME)

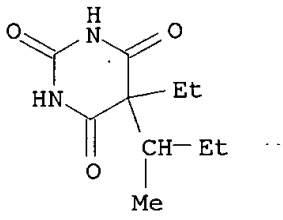


RN 115-44-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-(1-methylpropyl)-5-(2-propenyl)- (9CI)

(CA INDEX NAME)

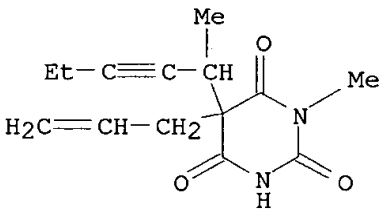


RN 143-81-7 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-(1-methylpropyl)-, monosodium salt (9CI) (CA INDEX NAME)



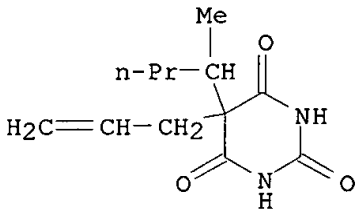
● Na

RN 309-36-4 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 1-methyl-5-(1-methyl-2-pentynyl)-5-(2-propenyl)-, sodium salt (9CI) (CA INDEX NAME)



● Na

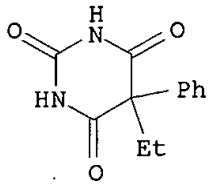
RN 309-43-3 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-(1-methylbutyl)-5-(2-propenyl)-, monosodium salt (9CI) (CA INDEX NAME)



● Na

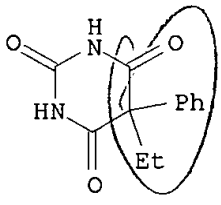
RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 18 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1999:775187 CAPLUS
DN 132:231813
TI NMDA- but not kainate-mediated events reduce efficacy of some antiepileptic drugs against generalized tonic-clonic seizures in mice
AU Urbanska, Ewa M.; Tomczyk, Tomasz; Haberek, Grzegorz; Pilip, Slawomir; Matyska, Joanna; Turski, Waldemar A.; Kleinrok, Zdzislaw; Czuczwar, Stanislaw J.
CS Department of Pharmacology and Toxicology, Medical University School, Lublin, 20-090, Pol.
SO Epilepsia (1999), 40(11), 1507-1511
CODEN: EPILAK; ISSN: 0013-9580
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB Purpose: The aim of this study was to evaluate the efficacy of conventional antiepileptic drugs (AEDs) against the generalized tonic-clonic seizures in mice subjected to the subconvulsive doses of N-methyl-D-aspartate (NMDA) or kainate. Methods: Mice were given NMDA and kainate in the doses of 50.0 and 9.0 mg/kg i.p., resp. [i.e., equal to 75% of their CD16 values (**convulsive** dose in 16% of the animals studied)]. Subsequently the anticonvulsive potential of conventional AEDs against the maximal electroshock-induced seizures was estd. Where necessary, the plasma levels of AEDs were assessed. Results: NMDA or kainate application did not affect the electroconvulsive threshold. NMDA, but not kainate, diminished the antiepileptic activity of diazepam (DZP) and carbamazepine (CBZ), increasing their 50% EDs (ED50s) from 14.1 and 8.6 to 19.0 and 12.1 mg/kg i.p., resp. Neither NMDA nor kainate affected the ED50 for valproate (VPA), phenobarbital (PB), or diphenylhydantoin (DPH) against electroconvulsions. NMDA-evoked effects were reversed with the use of the NMDA antagonist, D-(E)-2-amino-4-methyl-5-phosphono-3-pentenoic acid (CGP 40116) and were not accompanied by the alterations in the free plasma levels of AEDs. Conclusions: The NMDA-mediated events, but not kainate-related ones, seem to be involved in the protective action of DZP and CBZ against maximal electroshock-induced seizures. Moreover, it might be concluded that when subthreshold activation of NMDA receptors adds to other epileptogenic factors, DZP and CBZ are less efficacious. Presented data indicate that in such situations, adding the NMDA receptor antagonist (at very low doses) to the AED may yield beneficial **therapeutic** effects.
IT **50-06-6**, Phenobarbital, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(NMDA- but not kainate-mediated events reduce efficacy of antiepileptic drugs against generalized tonic-clonic seizures in mice in relation to combined use with NMDA antagonists)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)

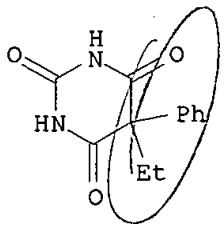


RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 19 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1999:621631 CAPLUS
DN 131:223407
TI Elevated plasma concentrations of homocysteine in antiepileptic drug treatment
AU Schwaninger, Markus; Ringleb, Peter; Winter, Ralph; Kohl, Brigitte; Fiehn, Walter; Rieser, Peter A.; Walter-Sack, Ingeborg
CS Department of Neurology, University of Heidelberg, Heidelberg, 69120, Germany
SO Epilepsia (1999), 40(3), 345-350
CODEN: EPILAK; ISSN: 0013-9580
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB Purpose: Homocysteine is an exptl. **convulsant** and an established risk factor in atherosclerosis. A nutritional deficiency of vitamin B6, vitamin B12, or folate leads to increased homocysteine plasma concns. During **treatment** with carbamazepine (CBZ), phenytoin, or phenobarbital, a deficiency in these vitamins is common. The objective of the study was to test the hypothesis that antiepileptic drug (AED) **treatment** is assocd. with increased homocysteine plasma concns. Methods: A total of 51 consecutive outpatients of our epilepsy clinic receiving stable, individually adjusted AED **treatment** and 51 sex- and age-matched controls were enrolled in the study. Concns. of total homocysteine and vitamin B6 were measured in plasma; vitamin B12 and folate were measured in the serum of fasted subjects. Results: Patients and controls differed significantly in concns. of folate (13.5.+-.1.0 vs. 17.4.+-.0.8 nM) and vitamin B6 (39.7.+-.3.4 vs. 66.2.+-.7.5 nM), whereas serum concns. of vitamin B12 were similar. The homocysteine plasma concn. was significantly increased to 14.7.+-.3.0 .mu.M in patients compared with controls (9.5.+-.0.5 .mu.M; $p < 0.05$, Wilcoxon rank-sum test). The no. of patients with concns. of >15 .mu.M was significantly higher in the patient group than among controls. The same result was obtained if only patients with CBZ monotherapy were included. Patients with increased homocysteine plasma concns. had lower folate concns. Conclusions: These data support the hypothesis that prolonged AED **treatment** may increase plasma concns. of homocysteine, although the alternative explanation that increased homocysteine plasma concns. are assocd. with the disease and not the **treatment** cannot be completely excluded at the moment.
IT **50-06-6**, Phenobarbital, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(elevated plasma concns. of homocysteine in humans on antiepileptic drug treatment)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)

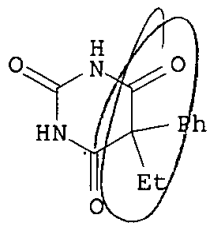


L20 ANSWER 20 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1999:275083 CAPLUS
DN 131:68015
TI Anticonvulsant efficacy of N-methyl-D-aspartate antagonists against convulsions induced by cocaine
AU Witkin, Jeffrey M.; Gasior, Maciej; Heifets, Boris; Tortella, Frank C.
CS Drug Development Group, Behavioral Neuroscience Branch, Addiction Research Center, National Institute on Drug Abuse, National Institutes of Health, Baltimore, MD, USA
SO Journal of Pharmacology and Experimental Therapeutics (1999), 289(2), 703-711
CODEN: JPETAB; ISSN: 0022-3565
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
AB **Convulsions** assocd. with cocaine abuse can be life threatening and resistant to std. emergency **treatment**. Cocaine (75 mg/kg, i.p.) produced clonic **convulsions** in .apprx.90% of male, Swiss-Webster mice. A variety of clin. used antiepileptic agents did not significantly protect against cocaine **convulsions** (e.g., diazepam and phenobarbital). Anticonvulsants in clin. practice that did significantly protect against **convulsion** did so only at doses with significant sedative/ataxic effects (e.g., clonazepam and valproic acid). In contrast, functional N-methyl-D-aspartate (NMDA) antagonists all produced dose-dependent and significant protection against the **convulsant** effects of cocaine. Anticonvulsant efficacy was achieved by blockade of both competitive and noncompetitive modulatory sites on the NMDA receptor complex. Thus, competitive antagonists, ion-channel blockers, polyamine antagonists, and functional blockers of the strychnine-insensitive glycine modulatory site all prevented cocaine seizures. The role of NMDA receptors in the control of cocaine-induced **convulsions** was further strengthened by the pos. correlation between the potencies of noncompetitive antagonists or competitive antagonists to block **convulsions** and their resp. affinities for their specific binding sites on the NMDA receptor complex. Although some NMDA blockers produced profound behavioral side effects at efficacious doses (e.g., noncompetitive antagonists), others (e.g., some low-affinity channel blockers, some competitive antagonists, and glycine antagonists) demonstrated significant and favorable sepn. between their anticonvulsant and side effect profiles. The present results provide the most extensive evidence to date identifying NMDA receptor blockade as a potential strategy for the discovery of agents for clin. use in averting toxic sequelae from cocaine overdose. Given the literature suggesting a role for these drugs in other areas of drug abuse **treatments**, NMDA receptor antagonists sit in a unique position as potential **therapeutic** candidates.
IT **50-06-6**, Phenobarbital, biological studies
RL: ADV (Adverse effect, including toxicity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(anticonvulsant efficacy of NMDA antagonists against cocaine-induced convulsions)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)



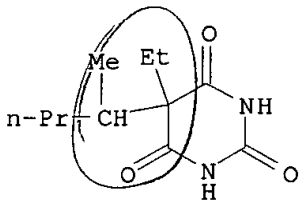
RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 21 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1999:256182 CAPLUS
DN 131:43105
TI Brain-derived neurotrophic factor immunoreactivity in the limbic system of rats after acute seizures and during spontaneous convulsions: temporal evolution of changes as compared to neuropeptide Y
AU Vezzani, A.; Ravizza, T.; Moneta, D.; Conti, M.; Borroni, A.; Rizzi, M.; Samanin, R.; Maj, R.
CS Laboratory of Experimental Neurology, Mario Negri Institute for Pharmacological Research, Milan, Italy
SO Neuroscience (Oxford) (1999), 90(4), 1445-1461
CODEN: NRSCDN; ISSN: 0306-4522
PB Elsevier Science Ltd.
DT Journal
LA English
AB Seizures increase the synthesis of brain-derived neurotrophic factor in forebrain areas, suggesting this neurotrophin has biol. actions in epileptic tissue. The understanding of these actions requires information on the sites and extent of brain-derived neurotrophic factor prodn. in areas involved in seizures onset and their spread. In this study, the authors investigated by immunocytochem. the changes in brain-derived neurotrophic factor in the hippocampus, entorhinal and perirhinal cortices of rats at increasing times after acute seizures eventually leading to spontaneous **convulsions**. The authors also tested the hypothesis that seizure-induced changes in brain-derived neurotrophic factor induce later modifications in neuropeptide Y expression by comparing, in each instance, their immunoreactive patterns. As early as 100 min after seizure induction, brain-derived neurotrophic factor immunoreactivity increased in CA1 pyramidal and granule neurons and in cells of layers II-III of the entorhinal cortex. At later times, immunoreactivity progressively decreased in somata while increasing in fibers in the hippocampus, the subicular complex and in specific layers of the entorhinal and perirhinal cortices. Changes in neuropeptide Y immunoreactivity were superimposed upon and closely followed those of brain-derived neurotrophic factor. One week after seizure induction, brain-derived neurotrophic factor and neuropeptide Y immunoreactivities were similar to controls in 50% of rats. In rats experiencing spontaneous **convulsions**, brain-derived neurotrophic factor and neuropeptide Y immunoreactivity was strongly enhanced in fibers in the hippocampus/parahippocampal gyrus and in the temporal cortex. In the dentate gyrus, changes in immunoreactivity depended on sprouting of mossy fibers as assessed by growth-assocd. protein-43-immunoreactivity. These modifications were inhibited by repeated anticonvulsant **treatment** with phenobarbital. The dynamic and temporally-linked alterations in brain-derived neurotrophic factor and neuropeptide Y in brain regions critically involved in epileptogenesis suggest a functional link between these two substances in the regulation of network excitability.
IT **50-06-6**, Phenobarbital, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(BDNF and neuropeptide Y immunoreactivity in spontaneously epileptic rat in relation to phenobarbital anticonvulsant treatment)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)



RE.CNT 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 22 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1999:228889 CAPLUS
DN 130:246315
TI Anticonculsants for soman-induced seizure activity
AU Shih, Tsung-Ming; McDonough, John H., Jr.; Koplovitz, Irwin
CS Pharmcology Drug Assessment Divisions, US Army Medical Research Institute Chemical Defense, Aberdeen Proving Ground, MD, 21010, USA
SO Journal of Biomedical Science (Basel) (1999), 6(2), 86-96
CODEN: JBCIEA; ISSN: 1021-7770
PB S. Karger AG
DT Journal
LA English
AB This report describes studies of anticonvulsants for the organophosphorus (OP) nerve agent soman: a basic research effort to understand how different pharmacol. classes of compds. influence the expression of seizure produced by soman in rats, and a drug screening effort to det. whether clin. useful antiepileptics can modulate soman-induced seizures in rats. Electroencephalog. (EEG) recordings were used in these studies. Basic studies were conducted in rats pretreated with HI-6 and challenged with 1.6 .times. LD50 soman. Antimuscarinic compds. were extremely effective in blocking (pretreatment) or terminating soman seizures when given 5 min after seizure onset. However, higher doses were required when **treatment** was delayed for >10 min, and some antimuscarinic compds. lost anticonvulsant efficacy when **treatment** was delayed for >40 min. Diazepam blocked seizure onset, yet seizures could recur after an initial period of anticonvulsant effect at doses .ltoreq.2.5 mg/kg. Diazepam could terminate ongoing seizures when given 5 min after seizure onset, but doses .ltoreq.20 mg/kg were ineffective when **treatment** was delayed for 40 min. The GABA uptake inhibitor, tiagabine, was ineffective in blocking or terminating soman motor **convulsions** or seizures. The Glue receptor antagonists, NBQX, GYKI 52466, and memantine, had weak or minimal antiseizure activity, even at doses that virtually eliminated signs of motor **convulsions**. The antinicotinic, mecamylamine, was ineffective in blocking or stopping seizure activity. Pretreatment with a narrow range of doses of .alpha.2-adrenergic agonist, clonidine, produced variable protection (40-60%) against seizure onset; **treatment** after seizure onset with clonidine was not effective. Screening studies in rats, using HI-6 pretreatment, showed that benzodiazepines (diazepam, midazolam, and lorazepam) were quite effective when given 5 min after seizure onset, but lost their efficacy when given 40 min after onset. The barbiturate, pentobarbital, was modestly effective in terminating seizures when given 5 or 40 min after seizure onset, while other clin. effective antiepileptic drugs, trimethadione and valproic acid, were only slightly effective when given 5 min after onset. In contrast, phenytoin, carbamazepine, ethosuximide, MgSO4, lamotrigine, primidone, felbamate, acetazolamide, and ketamine were ineffective.
IT **57-33-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(anticonvulsants for soman-induced seizure activity)
RN 57-33-0 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-(1-methylbutyl)-, monosodium salt (9CI) (CA INDEX NAME)



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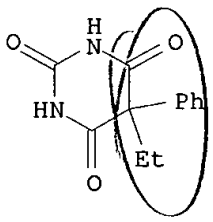
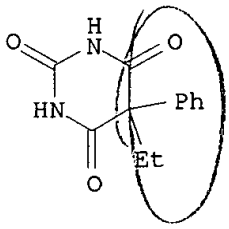
RE.CNT 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 23 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1999:195418 CAPLUS
DN 131:15061
TI Influence of intraperitoneal administration of tetanus toxin on experimental seizures and protection afforded by some antiepileptic drugs in mice
AU Korolkiewicz, R.; Gasior, M.; Mlynarczyk, M.; Petrusewicz, J.; Kleinrok, Z.
CS Department of Pharmacology, Medical University of Gdansk, Gdansk, 80-227, Pol.
SO Neuroscience Research Communications (1999), 24(1), 19-26
CODEN: NRCOEE; ISSN: 0893-6609
PB Wiley-Liss, Inc.
DT Journal
LA English
AB Our report aimed at describing the effects of the peripheral administration of tetanus toxin (Tetx) in clin. relevant doses on the functions of the central nervous system (CNS) in order to differentiate them with the consequences of central toxin administration. Tetx injected i.p. evoked death in 50 % of mice (LD50) at 11.0 (8.3-14.6) minimal LDs/kg (MLD/kg). Tetx (0.2/0.5 and 1.0 LD50) increased the **convulsant** thresholds of elec. current 24-144 h post-**treatment**. Tetx (0.5 LD50) applied 48/120 h before the tests, attenuated the potency of chem. **convulsants**, increasing protection by antiepileptics in maximal electroshock, without affecting their total plasma levels, .gamma.-aminobutyric acid concn. (GABA) and total L-glutamic acid decarboxylase activity (GAD) in brain homogenates-results similar to obtained after intracerebroventricular (i.c.v.) Tetx. These effects imply a preponderance of inhibitory over excitatory transmission, due probably to Tetx action at neuronal level. It indicates that Tetx penetrating into the central nervous system after i.p. injections evoke changes similar to those subsequent to i.c.v. Tetx administration, hinting that the two routes can have comparable predictive value in describing Tetx-induced changes in **convulsive** thresholds.
IT **50-06-6**, Phenobarbital, biological studies
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(influence of tetanus toxin on exptl. seizures and protection by antiepileptic drugs)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)

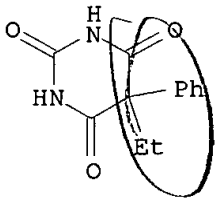


RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 24 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1998:625789 CAPLUS
DN 130:20493
TI A comparison of four **treatments** for generalized **convulsive** status epilepticus
AU Treiman, David M.; Meyers, Patti D.; Walton, Nancy Y.; Collins, Joseph F.; Colling, Cindy; Rowan, A. James; Handforth, Adrian; Faught, Edward; Calabrese, Vincent P.; Uthman, Basim M.; Ramsay, R. Eugene; Mamdani, Meenal B.
CS Neurology Services of the Veterans Affairs Medical Centers in West Los Angeles, CA, USA
SO New England Journal of Medicine (1998), 339(12), 792-798
CODEN: NEJMAG; ISSN: 0028-4793
PB Massachusetts Medical Society
DT Journal
LA English
AB A 5-yr randomized, double-blind, multicenter trial was conducted on 4 i.v. regimens: diazepam (0.15 mg/kg) followed by phenytoin (18 mg/kg); lorazepam (0.1 mg/kg); phenobarbital (15 mg/kg); and phenytoin (18 mg/kg). Patients were classified as having either overt generalized status epilepticus or subtle status epilepticus. **Treatment** was considered successful when all motor and electroencephalog. seizure activity ceased within 20 min after the beginning of the drug infusion and there was no return of seizure activity during the next 40 min. In group with overt generalized **convulsive** status epilepticus, lorazepam was successful in 64.9% of those assigned to receive it, phenobarbital in 58.2%, diazepam plus phenytoin in 55.8%, and phenytoin in 43.6%. Lorazepam was superior to phenytoin in a pairwise comparison. Among the patients with subtle generalized **convulsive** status epilepticus, no significant differences among the **treatments** were detected. In an intention-to-**treat** anal., the differences among **treatment** groups were not significant, either among the patients with overt status epilepticus or among those with subtle status epilepticus. There were no differences among the **treatments** with respect to recurrence during the 12-h study period, the incidence of adverse reactions, or the outcome at 30 days. Overall, as initial i.v. **treatment** for overt generalized **convulsive** status epilepticus, lorazepam is more effective than phenytoin. Although lorazepam is no more effective than phenobarbital or diazepam plus phenytoin, it is easier to use.
IT **50-06-6**, Phenobarbital, biological studies
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(antiepileptic activity in humans of diazepam vs. phenytoin vs. lorazepam vs.)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)

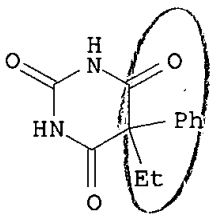


L20 ANSWER 25 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1998:523400 CAPLUS
DN 129:269814
TI Cellular mechanisms of anti-epileptic drugs revisited
AU Mutani, Roberto; Cantello, Roberto; Gianelli, Maria; Civardi, Carlo
CS Department of Neurology, University of Turin School of Medicine, Novara, 28100, Italy
SO Current Problems in Epilepsy (1997), 12(Molecular and Cellular Targets for Antiepileptic Drugs), 131-140
CODEN: CPEPES; ISSN: 0950-4591
PB John Libbey & Co. Ltd.
DT Journal; General Review
LA English
AB A review with 74 refs. Phenobarbital (PB), phenytoin (PHT), carbamazepine (CSZ), and ethosuximide (ESM) were either serendipitously or empirically developed. Each of these drugs, except for PB, was discovered to be an effective anti-epileptic drug (AED) by testing its efficacy in suppressing **convulsions** induced in lab. animals. Over the last decades, electrophysiol., biochem. and pharmacol. investigations have greatly improved our knowledge of the basic events responsible for epileptogenesis. These advances and the consideration that about 30% if epileptic patients are refractory to **treatment** with conventional AEDs, have stimulated the research toward the rational development of a new generation of AEDs. capable of producing a direct pharmacol. influence on some of the mechanisms underlying seizure generation and epileptogenesis. In this chapter we review some recent findings that are relevant for understanding the mechanisms of action of some conventional AEDs.
IT **50-06-6**, Phenobarbital, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(cellular mechanisms of anti-epileptic drugs revisited)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)



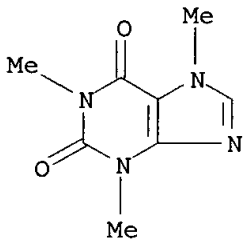
RE.CNT 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 26 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1998:481536 CAPLUS
DN 129:170466
TI Comparison of valproate and phenobarbital treatment after status epilepticus in rats
AU Bolanos, A. R.; Sarkisian, M.; Yang, Y.; Hori, A.; Helmers, S. L.; Mikati, M.; Tandon, P.; Stafstrom, C. E.; Holmes, G. L.
CS Department of Neurology, Harvard Medical School, Children's Hospital Boston, Boston, MA, 02115, USA
SO Neurology (1998), 51(1), 41-48
CODEN: NEURAI; ISSN: 0028-3878
PB Lippincott-Raven Publishers
DT Journal
LA English
AB To investigate the long-term effects of two widely used antiepileptic medications, valproate and phenobarbital, on learning and behavior in the kainic acid (KA) model of epilepsy. Prior clin. and animal studies have demonstrated that phenobarbital administered during development may result in subsequent cognitive impairment. It is unclear whether these adverse effects of phenobarbital extend to other antiepileptic drugs. A **convulsant** dose of KA was administered to rats on postnatal day (P) 35. From P36-75 rats received daily injections of phenobarbital (PH), valproate (VPA), or saline and spontaneous seizure frequency was monitored with video recordings. After tapering of the drugs, the rats were tested in the water maze (a measure of visuospatial memory) and handling test (a measure of emotionality). Brains were then analyzed for histol. lesions. KA caused status epilepticus in all the rats. In the PH- and saline-**treated** groups, there was impaired learning in the water maze, increased emotionality, recurrent seizures, and histol. lesions in the hippocampal areas CA3, CA1, and dentate hilus. However, VPA-**treated** rats had no spontaneous seizures, abnormalities in handling, or deficits in visuospatial learning, and had fewer histol. lesions than animals receiving KA alone. The long-term consequences of AED **treatment** during development are related to the drug used. VPA **treatment** after KA-induced status epilepticus prevents many of the neurol. sequelae typically seen after KA.
IT **50-06-6**, Phenobarbital, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(comparison of valproate and phenobarbital treatment after status epilepticus in rats)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)



RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

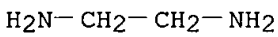
L20 ANSWER 27 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1998:448948 CAPLUS
DN 129:184172
TI Felbamate demonstrates low propensity for interaction with methylxanthines and Ca2+ channel modulators against experimental seizures in mice
AU Gasior, Maciej; Swiader, Mariusz; Przybylko, Marcin; Borowicz, Kinga; Turski, Waldemar A.; Kleinrok, Zdzislaw; Czuczwar, Stanislaw J.
CS Department of Pharmacology, Medical University School, Lublin, 20-090, Pol.
SO European Journal of Pharmacology (1998), 352(2/3), 207-214
CODEN: EJPHAZ; ISSN: 0014-2999
PB Elsevier Science B.V.
DT Journal
LA English
AB The aim of this study was to det. the interaction potential of the new antiepileptic drug felbamate (2-phenyl-1,3-propanediol dicarbamate) with three Ca2+ channel blockers (nicardipine, nifedipine, and flunarizine), one Ca2+ channel activator (Bay K 8644), and two methylxanthines (caffeine and aminophylline) which are all known to markedly change protective effects of conventional antiepileptic drugs. To do so, the maximal electroshock seizure test in mice (an exptl. model predicting drug efficacy in the **treatment** of human generalized tonic-clonic seizures) was employed to (1) quantify changes in the protective efficacy and potency of felbamate produced by adjunct drugs and (2) assess the ability of aminophylline and caffeine to affect protective efficacy afforded by a submaximal protective dose of felbamate against maximal electroshock-induced seizures. Doses of adjunct drugs were selected based on their effects on the threshold for electroconvulsions and on appropriate literature. Nicardipine (10-30 mg/kg), nifedipine (5-20 mg/kg), flunarizine (2.5-10 mg/kg), Bay K 8644 (2.5-5 mg/kg), and aminophylline (50-75 mg/kg) did not change the protective efficacy and potency of felbamate against maximal electroshock-induced tonic **convulsions**. Aminophylline in the dose of 100 mg/kg, however, diminished the protective potency of felbamate as evidenced by a statistically significant increase in the protective ED50 value of felbamate (a dose, in mg/kg, predicted to protect 50% of mice against **convulsive** stimulus) from 79.6 to 118 mg/kg; $P<0.05$. Aminophylline and caffeine only at high doses (100 and 161.7 mg/kg, resp.) significantly diminished the protective efficacy of felbamate (110 mg/kg) from 96% to 27% and 40% ($P<0.05$), resp. In conclusion, felbamate shows low interaction potential with Ca2+ channel modulators and methylxanthines. Such low interaction potential clearly differentiates felbamate from conventional antiepileptic drugs where protective effects are readily altered by the compds. tested in the present study.
IT **58-08-2**, Caffeine, biological studies **317-34-0**, Aminophylline
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(drug interaction potentials of antiepileptic felbamate)
RN 58-08-2 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3,7-trimethyl- (9CI) (CA INDEX NAME)



RN 317-34-0 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-, compd. with 1,2-ethanediamine (2:1) (9CI) (CA INDEX NAME)

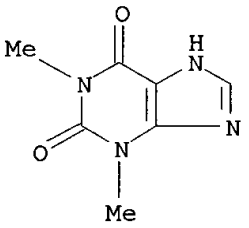
CM 1

CRN 107-15-3
CMF C2 H8 N2



CM 2

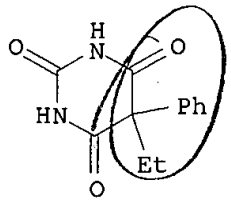
CRN 58-55-9
CMF C7 H8 N4 O2



RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

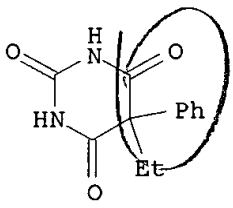
L20 ANSWER 28 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1998:417987 CAPLUS
DN 129:197849
TI Effect of 5-fluoroindole-2-carboxylic acid (an antagonist of the NMDA receptor-associated glycine site) on the anticonvulsive activity of conventional antiepileptic drugs
AU Kaminski, R.; Przywara, B.; Gasior, M.; Kleinrok, Z.; Czuczwar, S. J.
CS Department of Clinical Toxicology, Institute of Rural Medicine, Lublin, Pol.
SO Journal of Neural Transmission (1998), 105(2-3), 133-146
CODEN: JNTRF3; ISSN: 0300-9564
PB Springer-Verlag Wien
DT Journal
LA English
AB 5-Fluoroindole-2-carboxylic acid, an antagonist of the glycine site within the NMDA receptor complex, administered i.p. in doses of 150 and 200 mg/kg, 120 min before electroconvulsions, significantly raised the **convulsive** threshold from 6.8 to 7.9 and 8.3 mA, resp. At lower doses, it did not influence the threshold. However, lethality was obsd. 24 h after administration of the threshold-elevating doses of this glycine site antagonist. 5-Fluoroindole-2-carboxylic acid (100 mg/kg), applied together with carbamazepine, valproate or phenobarbital, significantly reduced their ED50 values against maximal electroshock - from 13.9 to 7.5 mg/kg, from 291 to 242 mg/kg, and from 18.6 to 11.1 mg/kg, resp. At the dose of 50 mg/kg, it also potentiated the protective activity of carbamazepine. However, 5-fluoroindole-2-carboxylic acid, up to 100 mg/kg, did not affect the anti-**convulsive** activity of diphenylhydantoin. When applied at doses equal to their ED50 values against maximal electroshock-induced **convulsions**, carbamazepine (13.9 mg/kg), phenobarbital (18.6 mg/kg) and valproate (291 mg/kg) did not affect the motor performance of mice in the chimney test. 5-Fluoroindole-2-carboxylic acid (100 mg/kg) produced a significant motor impairment, at 50 mg/kg it did not affect the motor performance. The combined **treatment** of 5-fluoroindole-2-carboxylic acid (100 mg/kg) with carbamazepine, phenobarbital or valproate, providing a 50% protection against maximal electroshock, resulted in motor impairment. Only the combination of 5-fluoroindole-2-carboxylic acid (50 mg/kg) with carbamazepine (8.6 mg/kg) did not significantly influence this parameter. Almost all of the antiepileptic drugs studied, when administered at doses equal to their ED50 values against maximal electroshock, did not influence retention in the passive avoidance task, which is a measure of long-term memory. Only valproate (291 mg/kg) worsened long-term memory. The combined **treatment** of 5-fluoroindole-2-carboxylic acid (100 mg/kg) with carbamazepine or phenobarbital, providing a 50% protection against maximal electroshock, did not affect the retention. The combination of 5-fluoroindole-2-carboxylic acid (100 mg/kg) with valproate (242 mg/kg) caused a significant impairment of long-term memory and mortality of 50% of animals 24 h following the administration. The results suggest that the blockade of the strychnine-insensitive glycine site may lead to an enhancement of the protective activity of some conventional antiepileptic drugs, which is assocd. with pronounced side-effects and lethality in some cases.
IT **50-06-6**, Phenobarbital, biological studies
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(fluoroindolecarboxylic acid potentiates anticonvulsive activity and toxicity of antiepileptic drugs)

RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)



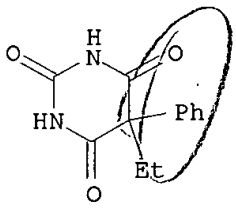
RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 29 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1998:258850 CAPLUS
DN 129:36121
TI Anticonvulsive and neurotoxic effects of lamictal (lamotrigine) in combination with other anticonvulsive preparations
AU Karpova, M. N.; Abrosimov, I. Yu.; Kryzhanovskii, G. N.; Raevskii, K. S.
CS Laboratory of Biochemistry, Laboratory of General Pathology of the Nervous System, Institute of General Pathology and Pathophysiology, Russian Academy of Medical Sciences, Moscow, Russia
SO Bulletin of Experimental Biology and Medicine (Translation of Byulleten Eksperimental'noi Biologii i Meditsiny) (1998), Volume Date 1997, 124(8), 744-746
CODEN: BEXBAN; ISSN: 0007-4888
PB Consultants Bureau
DT Journal
LA English
AB In the model of electroshock **convulsions** in mice, combined administration of lamictal with other anticonvulsants (sodium valproate, phenobarbital, diphenine, carbamazepine, ethosuximide, diazepam, and riodipine) decreased the ED50 of each single drug by 1.9-4.2-fold. The effectiveness of the lamictal/carbamazepine combination was the greatest. The potentiation of the anticonvulsant effects of the drugs by lamictal was accompanied by only additive neurotoxic interactions, so that the **therapeutic** index of the combinations was higher than that of the individual components.
IT **50-06-6**, Phenobarbital, biological studies
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(anticonvulsive and neurotoxic effects of lamotrigine in combination with)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)



RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 30 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1998:244492 CAPLUS
DN 129:23261
TI Effectiveness of combined application of calcium blockers and antiepileptic drugs
AU Karpova, M. N.; Abrosimov, I. Yu.; Kryzhanovskii, G. N.
CS Laboratory of Biochemistry, Laboratory of General Pathology of Nervous System, Institute of General Pathology and Pathophysiology, Russian Academy of Medical Sciences, Moscow, Russia
SO Bulletin of Experimental Biology and Medicine (Translation of Byulleten Eksperimental'noi Biologii i Meditsiny) (1997), 124(7), 661-664
CODEN: BEXBAN; ISSN: 0007-4888
PB Consultants Bureau
DT Journal
LA English
AB Using the model of electroshock **convulsions**, we showed that combined administration of blockers of potential-operated (riodipine and nifedipine) or receptor-activated (MK-801) calcium channels with the antiepileptics sodium valproate, phenobarbital, diazepam, ethosuximide, carbamazepine, and Diphenine markedly reduces drug doses and increases **therapeutic** index of their combinations.
IT **50-06-6**, Phenobarbital, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(effectiveness of combined application of calcium blockers and antiepileptic drugs)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)

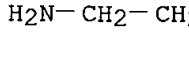


RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 31 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1997:754880 CAPLUS
DN 127:355205
TI Comparative evaluation of the neurotoxic potential of aminophylline and acepifylline in electroshock model of seizures and lethality in rats
AU Chakrabarti, A.; Saini, Harmsirat Kaur; Garg, S. K.
CS Dep. Pharmacology, Indira Gandhi Medical College, Shimla, 171001, India
SO Pharmacology Reviews and Communications (1997), 9(4), 223-228
CODEN: PHRCF6
PB Harwood Academic Publishers
DT Journal
LA English
AB Aminophylline (theophylline ethylenediamine) administered at a dose of 250 mg/kg (0.60 mmole/kg), i.p. produced severe tonic-clonic seizures and lethality in 100% of rats while at 100 mg/kg (0.24 mmole/kg), i.p., it did not produce any seizure or lethality and in intervening dose levels i.e., 150, 175, and 200 mg/kg (0.36, 0.42, and 0.48 mmole/kg, resp.) it showed a graded response to **convulsions** and lethality. Acepifylline (theophylline ethanoate of piperazine) did not produce any seizure or lethality in rats within the wide dose range of administration i.e., 250-1000 mg/kg, i.p. (0.44-1.76 mmole/kg). Aminophylline pretreatment (100 mg/kg or 0.24 mmole/kg, i.p. for 2 h) caused an increase in the electroshock induced **convulsions** and lethality rates and a decrease in the CI50 (i.e., the intensity of electroshock causing frank **convulsions** in 50% of rats) value for electroshock intensity compared to both the saline and acepifylline (140 mg/kg or 0.25 mmole/kg, i.p. for 2 h) pretreated groups of rats. Pretreatment with acepifylline caused slight increase in the electroshock induced **convulsion** rate without any lethality at comparable intensities of electroshock as compared to the saline **treated** group. The CI50 value for electroshock intensity was, however, decreased in the acepifylline pretreated group compared to the saline **treated** group of rats although the decrease was much less as compared to that with aminophylline pretreatment. The study established the neurotoxicity and neurosensitization with aminophylline. Acepifylline was found to have a greater neurosafety profile and therefore be safer for usage in asthmatic patients suffering from concomitant epilepsy or other seizure-prone neurol. deficits.
IT **317-34-0**, Aminophylline **18833-13-1**, Acepifylline
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(neurotoxic potential of aminophylline and acepifylline in electroshock model of seizures and lethality in rats)
RN 317-34-0 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-, compd. with 1,2-ethanediamine (2:1) (9CI) (CA INDEX NAME)

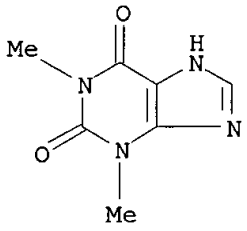
CM 1

CRN 107-15-3
CMF C2 H8 N2



CM 2

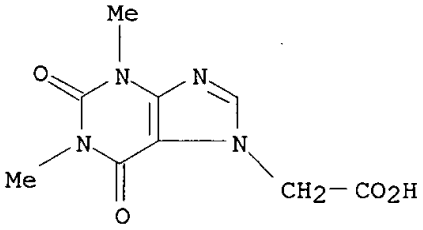
CRN 58-55-9
CMF C7 H8 N4 O2



RN 18833-13-1 CAPLUS
CN 7H-Purine-7-acetic acid, 1,2,3,6-tetrahydro-1,3-dimethyl-2,6-dioxo-, compd. with piperazine (9CI) (CA INDEX NAME)

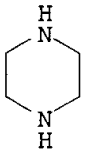
CM 1

CRN 652-37-9
CMF C9 H10 N4 O4

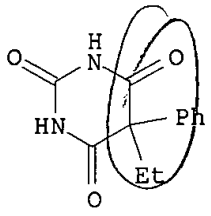


CM 2

CRN 110-85-0
CMF C4 H10 N2



L20 ANSWER 32 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1997:723168 CAPLUS
DN 128:10262
TI Cerebrospinal fluid and plasma pharmacokinetics of phenobarbital after intravenous administration to patients with status epilepticus
AU Brzakovic, B.; Pokrajac, M.; Dzoljic, E.; Levic, Z.; Varagic, V. M.
CS Department of Pharmacokinetics, Faculty of Pharmacy, University of Belgrade, Belgrade, Yugoslavia
SO Clinical Drug Investigation (1997), 14(4), 307-313
CODEN: CDINFR; ISSN: 1173-2563
PB Adis
DT Journal
LA English
AB The cerebrospinal fluid (CSF) and plasma pharmacokinetics of phenobarbital were studied after i.v. administration to 5 epileptic patients with **convulsive** status epilepticus and 6 seizure-free patients with newly diagnosed epilepsy. Phenobarbital (15 mg/kg) was infused at a rate of 100 mg/min. Plasma was collected prior to and throughout 24 h after drug administration. The CSF samples were obtained by lumbar puncture 2 h after the institution of phenobarbital infusion. Phenobarbital concns. in plasma and the CSF were measured by reversed-phase liq. chromatog. The plasma values of pharmacokinetic variables of distribution and elimination did not differ between the groups. Slightly lower phenobarbital concns. in the group of patients experiencing status epilepticus compared with seizure-free epileptic patients during the first hours after drug administration and the resultant elevated value of the rate const. of distribution (.alpha.) did not reach statistical significance, probably due to the small no. of participants in the study. Phenobarbital concns. were approx. 40% higher in the CSF of epileptic patients with status epilepticus compared with nonconvulsing subjects. The rate const. of phenobarbital distribution in the CSF (the ratio of the CSF concn. of the drug at time t1 and the area under the plasma concn.-time curve up to t1) in epileptic patients with status epilepticus exceeded that in seizure-free patients (0.29.+-.0.06h-1 vs 0.19.+-.0.05h-1, $p<0.05$). The study demonstrated statistically significantly higher phenobarbital concns. and more rapid appearance of phenobarbital in the CSF of epileptic patients with status epilepticus compared with nonconvulsing patients with epilepsy. The alteration in the pharmacokinetics of phenobarbitone in patients experiencing status epilepticus reported here addnl. supports the reported efficacy of i.v. phenobarbital in the **treatment** of this neurol. disorder.
IT **50-06-6**, Phenobarbital, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(cerebrospinal fluid and plasma pharmacokinetics of phenobarbital after i.v. administration to humans with status epilepticus)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)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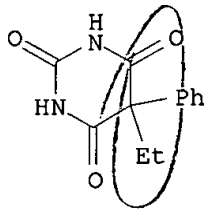
L20 ANSWER 33 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1997:530443 CAPLUS
DN 127:229511
TI Anticonvulsant and behavioral effects of neuroactive steroids alone and in conjunction with diazepam
AU Gasior, Maciej; Carter, Richard B.; Goldberg, Steven R.; Witkin, Jeffrey M.
CS Drug Development Group, Preclinical Pharmacology Laboratory, Addiction Research Center, National Institute on Drug Abuse, National Institutes of Health, Baltimore, MD, USA
SO Journal of Pharmacology and Experimental Therapeutics (1997), 282(2), 543-553
CODEN: JPETAB; ISSN: 0022-3565
PB Williams & Wilkins
DT Journal
LA English
AB Epilepsy continues to be a significant clin. problem as current medications neither adequately control seizures nor are free of untoward side-effects. Modulation of the neuroactive steroid site on the .gamma.-aminobutyric acid (GABA)A receptor complex may be an important new direction for pharmaceutical interventions in epilepsy. In this study we evaluated the protective actions of four neuroactive steroids, 3.alpha.-hydroxy-5.alpha.-pregnan-20-one, the 3.beta.-methylated analog, ganaxolone (3.alpha.-hydroxy-3.beta.-methyl-5.alpha.-pregnan-20-one), 3.alpha.-hydroxy-5.beta.-pregnan-20-one and Co 2-1068 (3.beta.-(4-acetylphenyl)ethynyl-3.alpha.,21-dihydroxy-5.beta.-20-one-21-hemisuccinate), against several std. **convulsive** tests in male, Swiss-Webster mice. Consistent with their GABAergic actions, the neuroactive steroids as well as diazepam and phenobarbital dose-dependently protected against clonic **convulsions** induced by pentylenetetrazol; the N-methyl-D-aspartate receptor antagonist, dizocilpine, was ineffective. In contrast to diazepam and phenobarbital, however, all of the neuroactive steroids and dizocilpine produced full protection against cocaine-induced **convulsions**. Some of the neuroactive steroids, as well as dizocilpine, were efficacious against the seizures and lethality induced by N-methyl-D-aspartate. Pregnenolone, a steroid devoid of GABAergic activity, was not effective in any of the **convulsant** models. Although all of the compds. produced motor toxicity in high doses as measured by the inverted-screen test, the neuroactive steroids demonstrated an equiv. or improved sepn. between anticonvulsant potency and motoric impairment. Inactive doses of the neuroactive steroids markedly enhanced the anticonvulsant effects of diazepam against pentylenetetrazol without significantly increasing motor toxicity. This adjunct **treatment** resulted in protective indexes ranging from 60 to 360 compared to 12 for diazepam alone. The distinct profile of anticonvulsant activity of the neuroactive steroids may be related to their combined actions on .gamma.-aminobutyric acid, N-methyl-D-aspartate receptors, or voltage-operated Ca++ channels. These results help to define the neuroactive steroids as a novel class of antiepileptic agents and suggest their potential in clin. practice.
IT **50-06-6**, Phenobarbital, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(anticonvulsant and behavioral effects of neuroactive steroids alone and in conjunction with diazepam)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)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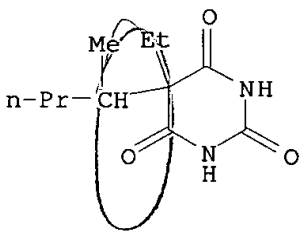
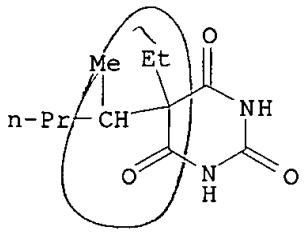
L20 ANSWER 34 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1997:458900 CAPLUS
DN 127:171471
TI Role of NMDA receptors in pentobarbital tolerance/dependence
AU Oh, Seikwan; Hoshi, Katsuji; Ho, I. K.
CS Department of Pharmacology and Toxicology, University of Mississippi Medical Center, Jackson, MS, 39216-4045, USA
SO Neurochemical Research (1997), 22(7), 767-774
CODEN: NEREDZ; ISSN: 0364-3190
PB Plenum
DT Journal
LA English
AB Effects of continuous pentobarbital administration on binding characteristics of [3H]MK-801 in the rat brain were examd. by autoradiog. Animals were rendered tolerant to pentobarbital using i.c.v. infusion of pentobarbital (300.mu.g/10.mu.l/h for 7 days) by osmotic minipumps and dependent by abrupt withdrawal from pentobarbital. The levels of [3H]MK-801 binding were elevated in rats 24-h after withdrawal from pentobarbital while there were no changes except in septum and anterior ventral nuclei in tolerant rats. For assessing the role of NMDA receptor in barbiturate action, an NMDA receptor antagonist, MK-801, was co-infused with pentobarbital. The pentobarbital-infused group had a shorter duration of pentobarbital-induced loss of righting reflex (sleeping time) than that of the control group, and MK-801 alone did not affect the righting reflex. However, co-infusion of MK-801 blocked hyperthermia, and prolonged the onset of **convulsions** induced by t-butylbicyclophosphorothionate (TBPS) in pentobarbital withdrawal rats. In addn., elevated [35S]TBPS binding was significantly attenuated by co-infusion with MK-801. These results suggest the involvement of NMDA receptor up-regulation in pentobarbital withdrawal and that the development of dependence can be attenuated by the **treatment** of subtoxic dose of MK-801.
IT **57-33-0**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(NMDA receptors role in pentobarbital tolerance/dependence)
RN 57-33-0 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-(1-methylbutyl)-, monosodium salt (9CI) (CA INDEX NAME)



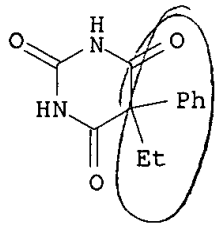
● Na

L20 ANSWER 35 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1997:154215 CAPLUS
DN 126:195190
TI Evaluation of anticonvulsant drugs for soman-induced seizure activity
AU Shih, Tsung-Ming; Mcdonough, John H. Jr.; Koplovitz, Irwin
CS Pharmacology and Drug Assessment Divisions, U.S. Army Medical Research Institute of Chemical Defense, MD, 21010-5425, USA
SO Journal of the American College of Toxicology (1996), 15(Suppl. 2), S43-S60
CODEN: JACTDZ; ISSN: 0730-0913
PB Lippincott-Raven
DT Journal
LA English
AB This report describes three lines of organophosphorus (OP) nerve-agent anticonvulsant studies: (a) a basic research effort to understand how different pharmacol. classes of compds. influence the expression of seizure produced by soman in rats, (b) a drug-screening effort to det. whether clin. useful antiepileptic drugs can modulate soman-induced seizures in rats, and (c) an advanced testing effort in which anticholinergic compds. are evaluated in comparison to the current anticonvulsant **treatment** (i.e., diazepam) in guinea pigs. Electroencephalog. (EEG) recordings were used in all studies. Basic studies were conducted in rats pretreated with HI-6 and challenged with 1.6 .times. the median LD (LD50) soman. Antimuscarinic compds. were extremely effective in blocking (pretreatment) or terminating soman seizures when given 5 min after seizure onset; however, significantly higher doses were required when **treatment** was delayed >10 min, and some antimuscarinic compds. lost anticonvulsant efficacy when **treatment** was delayed 40 min. Diazepam blocked seizure onset, yet seizures could recur after an initial period of anticonvulsant effect at doses .ltoreq.2.5 mg/kg. Diazepam could terminate ongoing seizures when given 5 min after seizure onset, but doses up to 20 mg/kg were ineffective when **treatment** was delayed for 40 min. The .gamma.-aminobutyric acid (GABA) uptake inhibitor tiagabine was ineffective in blocking or terminating soman motor **convulsions** or seizures. The glutamate receptor antagonists NBQX, GYKI 52466, and memantine had weak or minimal antiseizure activity, even at doses that virtually eliminated signs of motor **convulsions**. The antinicotinic mecamylamine was ineffective in blocking or stopping seizure activity. Pretreatment with a narrow range of doses of the alpha-2-adrenergic agonist clonidine produced variable protection (40-60%) against seizure onset; **treatment** after seizure onset with clonidine was not effective. Screening studies in rats, using HI-6 pretreatment, showed that the clin. effective antiepileptic drugs pentobarbital and valproic acid were modestly effective in terminating seizures when given shortly after seizure onset.
IT **57-33-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(evaluation of anticonvulsant drugs for soman-induced seizure activity)
RN 57-33-0 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-(1-methylbutyl)-, monosodium salt (9CI) (CA INDEX NAME)



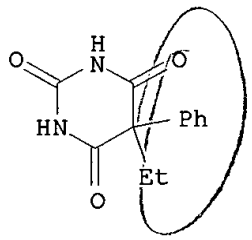
● Na

L20 ANSWER 36 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1996:502276 CAPLUS
DN 125:157783
TI Competitive NMDA receptor antagonists, LY 235959 and LY 233053, enhance the protective efficacy of various antiepileptic drugs against maximal electroshock-induced seizures in mice
AU Borowicz, Kinga K.; Gasior, Maciej; Kleinrok, Zdzislaw; Czuczwar, Stanislaw J.
CS Department Pharmacology and Toxicology, Lublin Medical University School, Lublin, PL-20-090, Pol.
SO Epilepsia (1996), 37(7), 618-624
CODEN: EPILAK; ISSN: 0013-9580
PB Lippincott-Raven
DT Journal
LA English
AB The objective of this study was to evaluate an interaction of two competitive N-methyl-D-aspartate (NMDA) receptor antagonists, LY 235959 [(-)-3R,4aS,6R,8aR-6-(phosphonomethyl)-decahydroisoquinoline-3-carboxylic acid; .ltoreq.0.5 mg/kg] or LY 233053 [cis-(.+-.)-4-[(2H-tetrazol-5-yl) methyl] piperidine-2-carboxylic acid; .ltoreq.5 mg/kg] with carbamazepine, diphenylhydantoin, phenobarbital, or valproate magnesium against maximal electroshock-induced **convulsions** in mice. Methods: Electroconvulsions were produced by means of an a.c. (ear-clip electrodes, 0.2-s stimulus duration, tonic hindlimb extension taken as the end point) delivered by a Hugo-Sachs stimulator (Type 221, Freiburg, FRG). Adverse effects were evaluated in the chimney test (motor performance) and passive-avoidance task (long-term memory). Plasma levels of antiepileptic drugs were measured by immunofluorescence. Results: Both LY 235959 and LY 233053 (.ltoreq.0.5 and 5 mg/kg, resp.) did not influence the electroconvulsive threshold but potentiated the anticonvulsant action of all antiepileptics studied. The combined **treatment** of LY 233053 (5 mg/kg) with carbamazepine, diphenylhydantoin, or phenobarbital (providing a 50% protection against maximal electroshock) resulted in the impairment of long-term memory. No adverse effects were obsd. with combinations of LY 235959 with these antiepileptics. The combined **treatment** of valproate with either LY 235959 or LY 233053 was superior to valproate alone, as regards motor impairment, but not the impairment of long-term memory. Neither NMDA-receptor antagonist elevated the total plasma levels of antiepileptic drugs studied. Conclusions: It may be concluded that NMDA-receptor blockade leads to the enhanced anticonvulsive action of conventional antiepileptics against maximal electroshock-induced seizures. A pharmacokinetic interaction does not seem probable.
IT **57-30-7**, Phenobarbital sodium
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(anticonvulsants interactions with NMDA antagonists LY 235959 and LY 233053)
RN 57-30-7 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl-, monosodium salt (9CI) (CA INDEX NAME)



● Na

L20 ANSWER 37 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1996:438670 CAPLUS
DN 125:104988
TI Therapeutic effects of zonisamide and some conventional antiepileptic drugs on amygdaloid kindling in rats
AU Hamada, Koichi; Song, Hong-Ki; Ishida, Shiro; Yagi, Kazuichi; Seino, Masakazu
CS National Epilepsy Center, Shizuoka Higashi Hospital, Shizuoka, 420, Japan
SO Journal of Brain Science (1996), 22(1), 7-15
CODEN: JBSCF5; ISSN: 1341-5301
PB Japan Brain Science Society
DT Journal
LA English
AB In this study, we compared the anticonvulsive effects of zonisamide (ZNS) with those of phenytoin (PHT), carbamazepine (CBZ) and phenobarbital (PB) in amygdaloid (AM) kindled rats. Electrodes were implanted into the left AM of adult male Wistar rats. The animals were kindled at the afterdischarge (AD) threshold. After the completion of kindling, the generalized seizure triggering threshold was detd. The drugs were administered i.p. in animals that showed stable generalized **convulsions** at near-threshold stimulation. Immediately after each drug trial, venous blood was sampled and the serum drug concn. was measured using EMIT or HPLC. All the drugs suppressed secondary generalization at lower doses, and further regressed the seizure stage and reduced the AD duration at higher doses. Higher doses of all drugs except ZNS, however, produced motor ataxia or lethargy. Thus, ZNS seemed to have a wider **therapeutic** range than other conventional antiepileptic drugs. An addnl. expt. on the effects of ZNS against supra-threshold stimulation suggested that a major action of ZNS in the kindling model is to attenuate the seizure spread rather than to elevate the AD threshold at the focus.
IT **50-06-6**, Phenobarbital, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(therapeutic effects of zonisamide and conventional antiepileptic drugs on amygdaloid kindling in rats)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)



L20 ANSWER 38 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1996:350450 CAPLUS
DN 125:114696
TI 1,4-Dihydroquinoxaline-2,3-diones as glycine receptor antagonists and their use as analgesics, anticonvulsants, neuroprotectants, and sedative-hypnotics
IN Weber, Eckard; Keana, John F. W.
PA Oregon Health Sciences University, USA; University of Oregon; Regents of the University of California
SO U.S., 116 pp., Cont.-in-part of U.S. Ser. No. 69,274, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5514680	A	19960507	US 1993-148259	19931105
	US 5631373	A	19970520	US 1994-289603	19940811
	IL 111533	A1	20010614	IL 1994-111533	19941106
	CA 2175795	AA	19950511	CA 1994-2175795	19941107
	WO 9512417	A1	19950511	WO 1994-US12775	19941107
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN				
	RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9511723	A1	19950523	AU 1995-11723	19941107
	AU 699353	B2	19981203		
	EP 732942	A1	19960925	EP 1995-902458	19941107
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 09504794	T2	19970513	JP 1994-513452	19941107
	NZ 276892	A	20000128	NZ 1994-276892	19941107
	US 5620979	A	19970415	US 1995-405708	19950317
	US 5622952	A	19970422	US 1995-405713	19950317
	FI 9601858	A	19960704	FI 1996-1858	19960502
	NO 9601770	A	19960705	NO 1996-1770	19960502
	US 5977107	A	19991102	US 1997-792872	19970131
	US 6147075	A	20001114	US 1999-376536	19990818
	US 6251903	B1	20010626	US 2000-661475	20000913
PRAI	US 1992-903080	B2	19920622		
	US 1992-995167	B2	19921222		
	US 1993-69274	B2	19930528		
	US 1993-148259	A2	19931105		
	US 1993-148268	B2	19931105		
	US 1994-208878	B2	19940311		
	US 1994-289603	A	19940811		
	WO 1994-US12775	W	19941107		
	US 1997-792872	A3	19970131		
	US 1999-376536	A3	19990818		

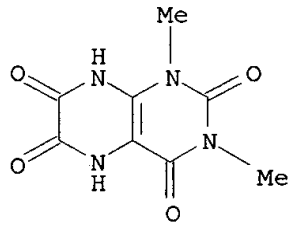
OS MARPAT 125:114696
AB Methods of **treating** or preventing neuronal loss assocd. with stroke, ischemia, CNS trauma, hypoglycemia and surgery, as well as **treating** neurodegenerative diseases including Alzheimer's disease, amyotrophic lateral sclerosis, Huntington's disease and Down's syndrome, **treating** or preventing the adverse consequences of the hyperactivity of the excitatory amino acids, as well as **treating**

anxiety, chronic pain, **convulsions**, inducing anesthesia and **treating** psychosis are disclosed, comprising administering to an animal in need of such **treatment** a title compd. I or a tautomer thereof; wherein R1 is halo, amino, hydroxylamino, acylamino, haloalkyl or nitro; R2 is amino, hydroxylamino, acylamino, nitro, haloalkyl or halo; R3 is halo, amino, hydroxylamino, acylamino or haloalkyl; and R4 is hydrogen, having high affinity for the glycine binding site, lacking PCP side effects and which crosses the blood brain barrier of the animal. Thus, e.g., cyclization of 4,5-dichloro-o-phenylenediamine with di-Et oxalate afforded 73.8% 6,7-dichloro-1,4-dihydro-2,3-quinoxalinedione; nitration with KNO3 afforded 89.6% 5-nitro-6,7-dichloro-1,4-dihydro-2,3-quinoxalinedione [I; R1 = NO2; R2 = R3 = Cl; R4 = H (II)] which was subjected to further purifn. and which exhibited affinity for the glycine binding site of 3.3 nM; the NO2 group in II increased, by several hundred fold, the glycine receptor affinity of its parent compd., 6,7-dichloro-1,4-dihydroquinoxaline-2,3-dione. II exhibited anticonvulsant activity, particularly in the audiogenic seizure model (ED50 = 5 mg/kg) and the NMDA-induced death model (ED50 = 20 mg/kg). Structure-activity relationships, as well as addnl. data on analgesic, ischemia-protectant, and sedative/hypnotic activities were presented. Pharmaceutical formulations were given.

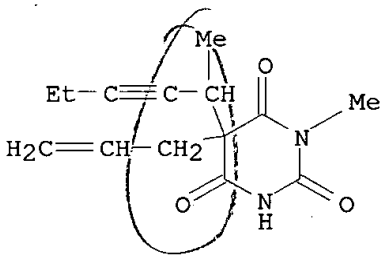
IT **5426-44-8P**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(1,4-dihydroquinoxaline-2,3-diones as glycine receptor antagonists and their use as analgesics, anticonvulsants, neuroprotectants, and sedative-hypnotics)

RN 5426-44-8 CAPLUS

CN 2,4,6,7(1H,3H)-Pteridinetetrone, 5,8-dihydro-1,3-dimethyl- (9CI) (CA INDEX NAME)

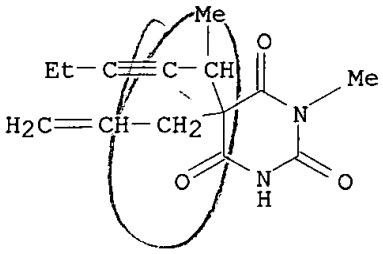


L20 ANSWER 39 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1995:870727 CAPLUS
DN 123:329826
TI Recovery after electroconvulsive therapy: Comparison of propofol with methohexitone anesthesia
AU Matters, R. M.; Beckett, W. G.; Kirkby, K. C.; King, T. E.
CS Royal Hobart Hospital, Tasmania, Australia
SO British Journal of Anaesthesia (1995), 75(3), 297-300
CODEN: BJANAD; ISSN: 0007-0912
PB Professional and Scientific Publications
DT Journal
LA English
AB We have studied prospectively 39 patients receiving a course of electroconvulsive therapy (ECT) for major depressive disorder; they were allocated randomly to receive either propofol or methohexitone for anesthesia. Recovery after the third ECT treatment was assessed by finger tap and digit symbol substitution tests at 15, 30, 45, 60 and 90 min after induction. Seizure duration (median (interquartile range)) was shorter with propofol (24 (10) s) than methohexitone (29 (17) s) (P = 0.08). There was no significant difference in psychometric recovery for drug type, duration of the seizure or initial severity of depression. These results suggest that the more rapid recovery rates noted with propofol in other procedures are not evident after elec. induced seizures.
IT **151-83-7**, Methohexitone
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(recovery after electroconvulsive therapy with propofol or methohexitone anesthesia)
RN 151-83-7 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 1-methyl-5-(1-methyl-2-pentynyl)-5-(2-propenyl)- (9CI) (CA INDEX NAME)

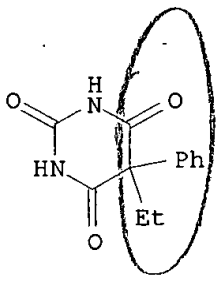


L20 ANSWER 40 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1995:865588 CAPLUS
DN 123:306426
TI The comparative effects of methohexital, propofol, and etomidate for electroconvulsive therapy
AU Avramov, Michail N.; Husain, Mustafa M.; White, Paul F.
CS Southwestern Medical Center, University Texas, Dallas, TX, USA
SO Anesthesia & Analgesia (Baltimore) (1995), 81(3), 596-602
CODEN: AACRAT; ISSN: 0003-2999
PB Williams & Wilkins
DT Journal
LA English
AB The i.v. anesthetics which are commonly used for electroconvulsive therapy (ECT) possess dose-dependent anticonvulsant properties. Since the clin. efficacy of ECT depends on the induction of a seizure of adequate duration, it is important to det. the optimal dose of the hypnotic for use during ECT. We compared the duration of seizure activity and cognitive recovery profiles after different doses of methohexital, propofol, and etomidate administered to induce hypnosis prior to ECT. Ten outpatients with major depressive disorders receiving maintenance ECT participated in this prospective, randomized, cross-over study. Patients were premedicated with glycopyrrolate, 0.2 mg i.v. (IV), and labetalol, 20-30 mg IV, and hypnosis was induced with an IV bolus injection of methohexital or propofol (0.75, 1.0, and 1.5 mg/kg), or etomidate (0.15, 0.2, and 0.3 mg/kg), administered over 10-15 s. Adequate muscle paralysis was achieved with succinylcholine, 1.0-1.4 mg/kg IV. Each patient's seizure threshold was detd. prior to enrollment in the study and the elec. stimulus variables were kept const. throughout the study period. After delivery of a bilateral elec. stimulus, the duration of the resulting electroencephalog. (EEG) and motor seizures were recorded. A total of 90 ECT treatments were evaluated. The durations of EEG and motor seizures were longest after etomidate and shortest after propofol. There were no significant dose-related differences in motor and EEG seizure durations (means .+-. SD) after the low, intermediate, and high doses of etomidate of 44 .+-. 11 and 77 .+-. 19, 43 .+-. 10 and 76 .+-. 34, 42 .+-. 16 and 78 .+-. 56 s, resp. Conversely, both methohexital and propofol, 0.75, 1.0, and 1.5 mg/kg, produced dose-dependent decreases in motor and EEG seizure durations (i.e., 37 .+-. 10 and 58 .+-. 12, 36 .+-. 8 and 62 .+-. 24, and 29 .+-. 13 and 48 .+-. 20 for methohexital; 34 .+-. 15 and 56 .+-. 29, 31 .+-. 8 and 50 .+-. 17, and 20 .+-. 6 and 33 .+-. 12 for propofol, resp.). The awakening times were similar, regardless of the hypnotic or dose administered. The rate of cognitive recovery was prolonged after ECT treatments with a longer duration of seizure activity. Discharge time was 5-7 min longer after etomidate than methohexital or propofol. Etomidate, 0.15-0.3 mg/kg, has minimal effect on the duration of ECT-induced seizure activity. However, recovery of cognitive functions was prolonged after etomidate because of the longer period of seizure activity. Propofol and methohexital, at doses more than 1 mg/kg, lead to 35%-45% decreases in ECT-induced seizure duration compared to etomidate. We conclude that etomidate may be a useful alternative to propofol and methohexital for ECT therapy.
IT **151-83-7**, Methohexital
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(comparative effects of methohexital, propofol, and etomidate for electroconvulsive therapy in humans)
RN 151-83-7 CAPLUS

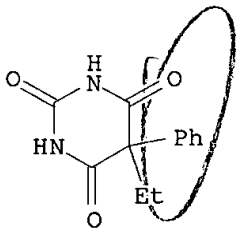
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 1-methyl-5-(1-methyl-2-pentynyl)-5-(2-propenyl)- (9CI) (CA INDEX NAME)



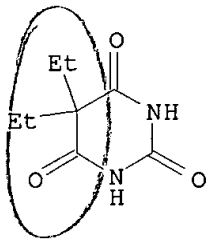
L20 ANSWER 41 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1995:751431 CAPLUS
DN 123:188331
TI The non-competitive AMPA/kainate receptor antagonist, GYKI 52466, potentiates the anticonvulsant activity of conventional antiepileptics
AU Borowicz, Kinga K.; Gasior, Maciej; Kleinrok, Zdzislaw; Czuczwar, Stanislaw J.
CS Department of Pharmacology and Toxicology, Lublin Medical University School, Jaczewskiego 8, Lublin, 20-090, Pol.
SO European Journal of Pharmacology (1995), 281(3), 319-26
CODEN: EJPHAZ; ISSN: 0014-2999
PB Elsevier
DT Journal
LA English
AB 1-(4-Aminophenyl)-4-methyl-7,8-methylenedioxy-5H-2,3-benzodiazepine hydro chloride (GYKI 52466), up to 5 mg/kg, did not influence the electroconvulsive threshold but potentiated the anticonvulsant activity of valproate, carbamazepine and diphenylhydantoin against maximal electroshock-induced **convulsions** in mice. No potentiation was obsd. in the case of phenobarbital. Moreover, this non-NMDA receptor antagonist did not influence the plasma levels of the antiepileptic drugs studied, so a pharmacokinetic interaction, in terms of total and free plasma levels, is not probable. The combined **treatment** of GYKI 52466 with either carbamazepine or diphenylhydantoin (providing a 50% protection against maximal electroshock) was devoid of significant side effects (motor and long-term memory impairment). Valproate applied at a dose equal to its ED50 caused serious worsening of motor coordination and long-term memory. It is noteworthy that the combined **treatment** of GYKI 52466 with valproate was superior to valproate alone, as regards adverse effects. The results suggest that concomitant administration of GYKI 52466 with some conventional antiepileptic drugs may offer a novel approach in the **treatment** of epilepsy.
IT **50-06-6**, Phenobarbital, biological studies
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(potentiation of antiepileptics by non-NMDA receptor antagonist GYKI 52466)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)



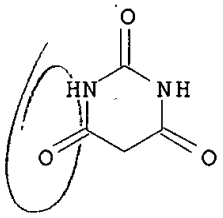
L20 ANSWER 42 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1995:740355 CAPLUS
DN 123:188206
TI Northern epilepsy syndrome: clinical course and the effect of medication on seizures
AU Hirvasniemi, Aune; Herrala, Pirjo; Leisti, Jaakko
CS Department Pediatrics, Kainuu Central Hospital, Kajaani, Finland
SO Epilepsia (1995), 36(8), 792-7
CODEN: EPILAK; ISSN: 0013-9580
PB Lippincott-Raven
DT Journal
LA English
AB We describe the clin. course and **treatment** of 19 patients with the Northern epilepsy syndrome, an autosomal recessively inherited epilepsy with assocd. mental deterioration. The clin. course could be divided into three successive stages. The first stage continued from the onset of epilepsy until puberty. Seizures began at a mean age of 6.6 yr and consisted predominantly of generalized tonic-clonic **convulsions** (GTC) and, transiently, also of complex partial seizures (CPS). Until puberty, seizure frequency increased in most patients from one attack in 1-2 mo to one to two attacks weekly. Seizures did not respond to phenytoin (PHT) or carbamazepine (CBZ), were transiently controlled by valproate (VPA) and phenobarbital (PB), but were effectively **treated** only by clonazepam (CZP). Mental deterioration began 2-5 yr after the onset of epilepsy and was most rapid before adulthood, a time when the seizures were also most frequent. The first signs of motor clumsiness also appeared then. The third stage was one of permanent disability and usually began in middle age. Seizures were few, but the patients were clumsy and had marked equil. difficulties.
IT **50-06-6**, Phenobarbital, biological studies
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(Northern epilepsy syndrome and clin. course in humans and the effect of medication on seizures)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)



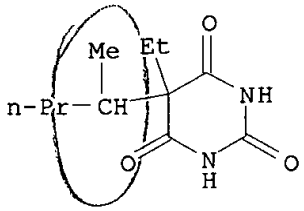
L20 ANSWER 43 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1995:297042 CAPLUS
DN 122:71870
TI Tolerance to competitive NMDA antagonists, but no cross-tolerance with barbiturates
AU Rabbani, M.; Wright, E. J.; Little, H. J.
CS Pharmacology Department, Medical School, Bristol, BS8 1TD, UK
SO Pharmacology, Biochemistry and Behavior (1995), 50(1), 9-15
CODEN: PBBHAU; ISSN: 0091-3057
PB Elsevier
DT Journal
LA English
AB Tolerance occurred to the sedative actions of the competitive NMDA antagonists, CGP39551 and CGP37849, as measured by a decrease in spontaneous locomotor activity after 1 wk or 2 wk of administration, resp., in studies using the TO strain of mice. Cross-tolerance was seen between these compds. When CGP37849 was given after 2 wk **treatment** with CGP39551, an increase in locomotor activity was seen. Chronic barbiturate **treatment**, producing tolerance to the actions of pentobarbitone, did not affect the sedative properties of CGP39551 or CGP37849. Chronic **treatment** with CGP39551 did not alter the ataxic actions of pentobarbitone. Seven days of **treatment** with HA966 (a weak partial agonist at the glycine site on the NMDA comples) caused complete tolerance to its sedative actions, but no cross-tolerance was seen to pentobarbitone, CGP39551, or CGP37849. A small but significant decrease was seen in the **convulsion** thresholds to NMDA after 15 days of **treatment** with CGP39551, and a small significant increase in ratings of **convulsive** behavior after 16 days of injections of CGP37849. No significant changes were found in either Bmax or Kd for [3H]-MK-801 binding in cerebrocortical tissue 24 h after the last chronic **treatment** with either of the NMDA antagonists.
IT **57-44-3**, Barbitone **67-52-7D**, Barbituric acid, derivs.
76-74-4, Pentobarbitone
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(cross-tolerance between barbiturates and NMDA antagonists)
RN 57-44-3 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5,5-diethyl- (9CI) (CA INDEX NAME)



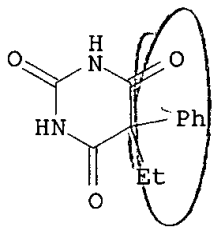
RN 67-52-7 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione (9CI) (CA INDEX NAME)



RN 76-74-4 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-(1-methylbutyl)- (9CI) (CA INDEX NAME)



L20 ANSWER 44 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1994:671903 CAPLUS
DN 121:271903
TI A new, non-pharmacologic model of convulsive status epilepticus induced by electrical stimulation: behavioral/electroencephalographic observations and response to phenytoin and phenobarbital
AU Handforth, Adrian; Treiman, David M.
CS Neurology Service, Department Veterans Affairs Medical Center, West Los Angeles, Los Angeles, CA, 90024, USA
SO Epilepsy Research (1994), 19(1), 15-25
CODEN: EPIRE8; ISSN: 0920-1211
DT Journal
LA English
AB Much remains to be learned about mechanisms underlying entry into, and temporal progression of, status epilepticus (SE). This report describes a non-pharmacol. model of generalized **convulsive** SE in rat. Pulsed trains of suprathreshold elec. current were administered bilaterally to either of four rostral forebrain sites: orbital cortex, medial precentral cortex, deep prepiriform cortex, or rostral caudate-putamen (per site). This induction method resulted in 30/32 animals attaining limb-clonic **convulsive** SE within a mean of 30-35 min for each forebrain site, with no differences between sites. Subsequent SE proceeded without further interventions, permitting observation of the natural course of progression. A stereotyped behavioral/electrog. sequence occurred, characterized by devolution. Behaviorally, animals progressed from predominantly limb clonus to head clonus, then to subtle twitching, and finally to elec. SE before cessation of spikes. The corresponding electrog. progression was from fast and slow spiking to periodic epileptiform discharges (PEDs). In 20 animals surviving to 48 h, pathol. damage affected mainly limbic sites; damage was related to total **convulsive** time rather than to clonic activity. High-dose phenobarbital but not phenytoin suppressed SE when given during orbital cortex-induced limb-clone SE. These findings are compatible with human observations and indicate that this model will enable investigations of generalized SE mechanisms and evaluation of new **therapeutic** agents for refractory SE.
IT **50-06-6**, Phenobarbital, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(new non-pharmacol. model of convulsive status epilepticus induced by elec. stimulation with behavioral/electroencephalog. observations and response to phenytoin and phenobarbital)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)



L20 ANSWER 45 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1994:671826 CAPLUS
DN 121:271826
TI Influence of chronic aminophylline on antielectroshock activity of diazepam and aminophylline-induced convulsions in mice
AU Wlaz, Piotr; Rolinski, Zbigniew; Kleinrok, Zdzislaw; Czuczwar, Stanislaw J.
CS Veterinary Fac., Sch. Agriculture, Lublin, PL-20-033, Pol.
SO Pharmacology, Biochemistry and Behavior (1994), 49(3), 609-13
CODEN: PBBHAU; ISSN: 0091-3057
PB Elsevier
DT Journal
LA English
AB The effects of chronic administration of aminophylline (AMPH; 50 mg/kg, twice daily for 14 consecutive days) were studied on both antielectroshock efficacy of diazepam (DZP) and **convulsive** activity of AMPH in mice. AMPH injected acutely at a dose of 50 mg/kg significantly reduced anticonvulsant action of DZP elevating ED50 from 10.9 (control) to 15.9 mg/kg. After the administration of AMPH for 3 days, ED50 value was still higher compared with control. Chronic **treatment** with AMPH resulted in further increase of ED50 of DZP, which was 20.2 mg/kg, and this elevation was (0.05, and 0.001, resp.). Therefore, no tolerance to this AMPH-mediated effect was found, and even an enhancing influence was obsd. Chronic **treatment** with AMPH decreased **convulsive** activity of AMPH elevating ED50 for induction of clonic seizures from 218 to 252 mg/kg. The remaining seizure parameters were unaffected. Furthermore, in both cases pharmacokinetic interactions were excluded, at least in terms of total plasma levels of the drugs. The results suggest that the mechanisms governing AMPH-induced reversal of the anticonvulsant efficacy of DZP qual. differ from those underlying AMPH-induced **convulsions**. Moreover, these data support the claim that AMPH should be avoided in patients suffering from different types of epilepsy.
IT **317-34-0**, Aminophylline
RL: ADV (Adverse effect, including toxicity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(influence of chronic aminophylline on antielectroshock activity of diazepam and aminophylline-induced convulsions in mice)
RN 317-34-0 CAPLUS
CN 1H-Purine-2,6-dione, 3,7-dihydro-1,3-dimethyl-, compd. with 1,2-ethanediamine (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 107-15-3
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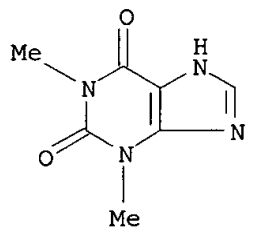
$H_2N-CH_2-CH_2-NH_2$

CM 2

CRN 58-55-9
CMF C7 H8 N4 O2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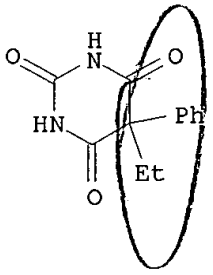
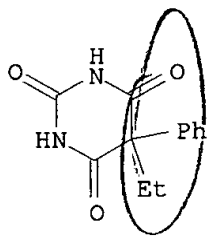
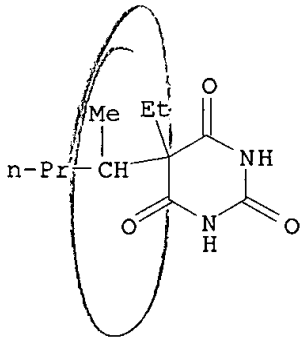
L20 ANSWER 46 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1994:449993 CAPLUS
DN 121:49993
TI The competitive NMDA antagonist, D-CPP-ene, potentiates the anticonvulsant activity of conventional antiepileptics against maximal electroshock-induced seizures in mice
AU Zarnowski, T.; Kleinrok, Z.; Turski, W. A.; Czuczwar, S. J.
CS Dep. Pharm., Med. Sch. Jaczewskiego, Lublin, PL-20-090, Pol.
SO Neuropharmacology (1994), 33(5), 619-24
CODEN: NEPHBW; ISSN: 0028-3908
DT Journal
LA English
AB D-CPP-ene [3-(2-carboxypiperazine-4-yl)-1-propenyl-1-phosphonic acid; a competitive antagonist of N-methyl-D-aspartic acid] in a dose of 2 mg/kg (i.p.) significantly increased the threshold for electroconvulsions. When given in a dose half that affecting the electroconvulsive threshold, D-CPP-ene potentiated the anticonvulsant activity of carbamazepine, diazepam, diphenylhydantoin, phenobarbital and valproate against maximal electroshock (50 mA)-induced seizures in mice. However, this NMDA antagonist did not influence the plasma levels of the antiepileptic drugs studied, so a pharmacokinetic interaction, in terms of total plasma levels at least, is not probable. The chimney test and retention testing in mice revealed that the combined **treatment** of D-CPP-ene at 1.0 mg/kg (i.p.) with either diazepam, diphenylhydantoin, phenobarbital or valproate (providing a 50% protection against maximal electroshock **convulsions**) resulted in motor impairment and caused impairment of long-term memory. On the other hand, a combination of D-CPP-ene and carbamazepine was devoid of adverse effects. It can be concluded that the potential utility of D-CPP-ene in combination with conventional antiepileptic drugs does not seem promising, except for carbamazepine.
IT **50-06-6**, Phenobarbital, biological studies
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(anticonvulsant activity of, by NMDA antagonist D-CPP-ene potentiation of)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)



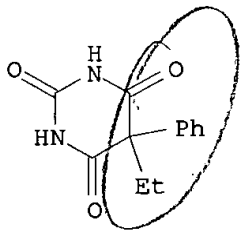
L20 ANSWER 47 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1994:69429 CAPLUS
DN 120:69429
TI Competitive NMDA receptor antagonists enhance the antielectroshock activity of various antiepileptics
AU Pietrasiewicz, Teresa; Czechowska, Grazyna; Dziki, Marek; Turski, Waldemar A.; Kleinrok, Zdzislaw; Czuczwar, Stanislaw J.
CS Dep. Pharmacol. Toxicol., Med. Sch., Lublin, 20-090, Pol.
SO European Journal of Pharmacology (1993), 250(1), 1-7
CODEN: EJPHAZ; ISSN: 0014-2999
DT Journal
LA English
AB CGP 37849 (1 mg/kg i.p.) enhanced the protective action of carbamazepine, diphenylhydantoin and phenobarbital against maximal electroshock-induced **convulsions** in mice. At 0.25 mg/kg CGP 37849 was inactive and at 0.5 mg/kg it potentiated the anticonvulsive activity of phenobarbital. CGP 39551 (5 mg/kg i.p.) reduced the ED50 values of diphenylhydantoin and phenobarbital, being without influence on carbamazepine. In the dose of 1.25 mg/kg, CGP 39551 potentiated the antielectroshock action of diphenylhydantoin and at 2.5 mg/kg that of phenobarbital. Neither NMDA receptor antagonist elevated the total plasma levels of antiepileptic drugs. Consequently, a pharmacokinetic interaction (in terms of total plasma levels at least) seems unlikely to be responsible for the obsd. potentiation of the antiepileptic drugs' activity. Combination of CGP 37849 with either carbamazepine or phenobarbital resulted in a motor and memory impairment quantified by the chimney test and passive avoidance task, resp. Moreover, combined **treatment** with phenobarbital and CGP 39551 caused a memory deficit. In contrast, diphenylhydantoin combined with either CGP 37849 or 39551 was devoid of adverse effects. It may be concluded that NMDA receptor blockade results in enhanced anticonvulsive action of common antiepileptics against maximal electroshock-induced seizures.
IT **50-06-6**, Phenobarbital, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(anticonvulsant activity of, NMDA antagonist CGP 37849 potentiation of)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)



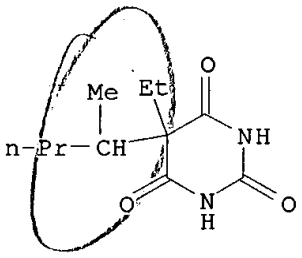
L20 ANSWER 48 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1992:626181 CAPLUS
DN 117:226181
TI Inhibitory influence of morphinans on ictal and interictal EEG changes induced by cortical application of penicillin in rabbits: a comparative study with NMDA antagonists and pentobarbitone
AU Zeng, Y. C.; Pezzola, A.; Scotti de Carolis, A.; Sagratella, S.
CS Pharmacol. Dep., Ist. Super. Sanita, Rome, 00161, Italy
SO Pharmacology, Biochemistry and Behavior (1992), 43(2), 651-6
CODEN: PBBHAU; ISSN: 0091-3057
DT Journal
LA English
AB The effects of dextrorphan (DX) and dextromethorphan (DM) were tested using the EEG and behavioral effects induced by topical cortical application of penicillin in rabbits. For comparison, the influence of the NMDA antagonists, dizocilpine (MK 801) and 3-((.+-.-2-carboxypiperazine-4-yl)propyl-1-phosphonic acid (CPP), and of pentobarbitone was investigated. Intracortical injection of 500 IU of penicillin produced an EEG spiking followed by a repeated generalization of the elec. and behavioral symptoms. Within a few minutes, DX (5-15 mg/kg, i.v.) or pentobarbitone (5-10 mg/kg, i.v.) reduced dose dependently and significantly ($p < 0.01$) the interictal and ictal EEG and behavioral effects elicited by cortical injection of 500 IU of penicillin. Higher doses of pentobarbitone (20 mg/kg, i.v.) but not of DX (20 mg/kg, i.v.) completely blocked the ictal behavioral and EEG effects elicited by cortical injection of 500 IU of penicillin. Within a few minutes, MK 801 (0.1-0.2 mg/kg, i.v.) or CPP (10-20 mg/kg, i.v.) reduced dose dependently and significantly ($p < 0.01$) the ictal EEG and behavioral effects elicited by cortical injection of 500 IU of penicillin, while they did not affect the penicillin-induced interictal EEG changes. Higher doses of MK 801 (0.3 mg/kg, i.v.) completely blocked the ictal behavioral and EEG effects elicited by cortical injection of 500 IU of penicillin. Within a few minutes, DM (10-20 mg/kg, i.v.) blocked the behavioral effects, but failed to affect either the interictal or the ictal EEG effects induced by cortical injection of 500 IU of penicillin. The data promote an involvement of NMDA receptors in the elec. and behavioral generalization of the epileptiform activity elicited by penicillin in rabbits. The results also indicate that morphinans might be successfully used for the acute **treatment** of epileptic and **convulsive** phenomena.
IT **76-74-4**, Pentobarbitone
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(anticonvulsant activity of, in penicillin model, morphinans in comparison with)
RN 76-74-4 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-(1-methylbutyl)- (9CI) (CA INDEX NAME)



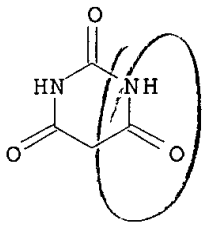
L20 ANSWER 49 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1989:18804 CAPLUS
DN 110:18804
TI A possible role for spinal noradrenaline in the mechanisms of 6-hydroxdopamine against pentylenetetrazol induced convulsions in rats
AU Abed, Wadie T.
CS Fac. Med., Jordan Univ. Sci. Technol., Irbid, Jordan
SO Life Sciences (1988), 43(22), 1831-6
CODEN: LIFSAK; ISSN: 0024-3205
DT Journal
LA English
AB The threshold of the generalized clonic **convulsions** induced by i.v. infusion of pentylenetetrazol (PTZ) was increased by the i.p. administration of the noradrenaline (NA) neurotoxin, 6-hydroxydopamine, which produced no changes in the levels of catecholamines in discrete areas of rat brain, but the effect was accompanied by spinal depletion of NA. Moreover, the anticonvulsant effects of phenobarbitone (PB) and diphenylhydantoin (DPH) against PTZ **convulsions** were also increased in the animals pretreated with 6-OHDA. The obsd. elevation of PTZ **convulsive** threshold and the potentiation of the anticonvulsant activity of PB and DPH in 6-OHDA **treated** rats were possibly mediated through the spinal cord depletion of NA.
IT **50-06-6**, Phenobarbitone, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(anticonvulsant activity of, noradrenaline of spinal cord modulation of)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)



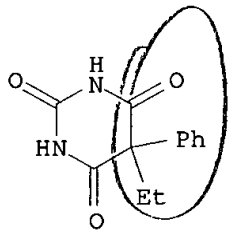
L20 ANSWER 50 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1988:486238 CAPLUS
DN 109:86238
TI Changes in benzodiazepine/GABA receptor complex function in benzodiazepine-tolerant mice
AU Nutt, David J.; Taylor, Stuart C.; Little, Hilary J.; Standing, Beth L.; Gale, Richard G.
CS Dep. Pharmacol., Univ. Oxford, Oxford, OX1 3QT, UK
SO Psychopharmacology (Berlin, Germany) (1988), 95(3), 407-12
CODEN: PSCHDL; ISSN: 0033-3158
DT Journal
LA English
AB Mice were given flurazepam (40 mg/kg, i.p.) once daily for 7 consecutive days. Twenty-four and forty-eight hours after the last injection measurements were made of the effects on **convulsion** threshold, body temp. and locomotor activity, of drugs acting on the GABA receptor complex. Decreases were seen in the hypothermic and hypomobility effects of progabide at 48 h, but no changes were seen in the effects of pentylenetetrazole or pentobarbitone. The actions of picrotoxin in all 3 types of test and the **convulsant** action of bicuculline (IP) were decreased at 24 h but not at 48 h. The **convulsive**, but not the hypothermic, effects of picrotoxin were increased at the 48 h interval. Apparently, chronic benzodiazepine **treatment** decreased some aspects of GABA receptor function at 48 h after the last dose; however, such an effect probably does not explain the previously reported increases in the effects of inverse agonists following chronic agonist **treatment**.
IT **76-74-4**, Pentobarbitone
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(pharmacol. of, benzodiazepine tolerance and GABA receptor function in relation to)
RN 76-74-4 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-(1-methylbutyl)- (9CI) (CA INDEX NAME)



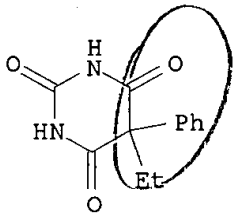
L20 ANSWER 51 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1988:124348 CAPLUS
DN 108:124348
TI Anticonvulsive activity of hydroxylamine derivatives of barbituric acid in the pentylenetetrazole convulsion test
AU Getova, D.
CS Dep. Exp. Pharmacol., Inst. Physiol., Sofia, Bulg.
SO Doklady Bolgarskoi Akademii Nauk (1987), 40(10), 131-4
CODEN: DBANAD; ISSN: 0366-8681
DT Journal
LA English
AB In mice with pentylenetetrazole-induced **convulsions**, all 7 title compds. administered at 1/6 of the LD50, prolonged the latency period before **convulsions**. Five of the compds. had **therapeutic** indexes (8.5-17.4) greater than those of the ref. compds. (e.g. phenobarbital).
IT **67-52-7D**, Barbituric acid, hydroxylamine derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(anticonvulsant activity of)
RN 67-52-7 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione (9CI) (CA INDEX NAME)



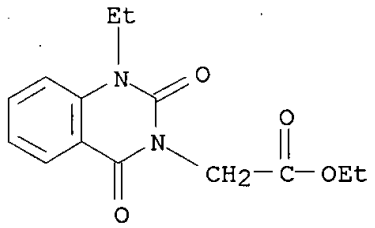
L20 ANSWER 52 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1988:31330 CAPLUS
DN 108:31330
TI Effect of aminophylline and enprofylline on the protective efficacy of common antiepileptic drugs against electroconvulsions in mice
AU Czuczwar, Stanislaw J.; Kleinrok, Zdzislaw; Turski, Lechoslaw; Turski, Waldemar A.
CS Dep. Pharmacol., Med. Sch., Lublin, PL-20090, Pol.
SO Epilepsia (1987), 28(4), 383-6
CODEN: EPILAK; ISSN: 0013-9580
DT Journal
LA English
AB The anticonvulsant potency of phenobarbital (PB) (120 min before the test), phenytoin (PHT) (120 min), carbamazepine (CBZ) (60 min), valproate (VPA) (30 min), and acetazolamide (60 min) alone or in combination with either aminophylline (50 mg/kg, 30 min) or enprofylline (46.2 mg/kg, 30 min) (all administered i.p.) was measured against maximal electroshock-induced **convulsions** in mice. Aminophylline decreased anticonvulsant activity of PB, PHT, CBZ, and VPA, increasing the resp. ED50 values. Enprofylline in an equimolar dose did not exert such an effect. Neither aminophylline nor enprofylline affected the anticonvulsant action of acetazolamide. The data favor enprofylline as a preferable drug for **treatment** of obstructive lung diseases in epilepsy patients.
IT **50-06-6**, Phenobarbital, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(anticonvulsant activity of, aminophylline or enprofylline effects on)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)



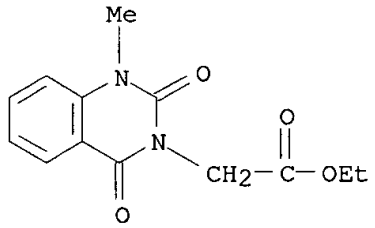
L20 ANSWER 53 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1988:482 CAPLUS
DN 108:482
TI The effect of repeated seizures on anticonvulsant drug response in the kindling model
AU Mace, J. A.; Burnham, W. M.
CS Dep. Pharmacol., Univ. Toronto, Toronto, ON, M5S 1A8, Can.
SO Electroencephalography and Clinical Neurophysiology (1987), 67(2), 171-5
CODEN: ECNEAZ; ISSN: 0013-4694
DT Journal
LA English
AB Drug response (ED50) was measured in rats after either a small or a large no. of pretreatment seizures, administered in the kindling paradigm. A variety of expts. were performed: different drugs (phenobarbital, phenytoin, and carbamazepine); different seizures types (amygdala focal seizure, cortical focal seizure, generalized **convulsion**); and different stimulation parameters. In no case were seizures found to be harder to suppress following repeated pretreatment seizures. After large nos. of pretreatment seizures (40 or 100), drug response was actually enhanced. These data indicate that the mere repetition of seizures does not automatically lead to a decrease in anticonvulsant effectiveness. They offer no particular rationale for the early initiation of anticonvulsant **therapy** in clin. situations.
IT **50-06-6**, Phenobarbital, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(anticonvulsant activity of, repeated seizure from kindling effect on)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)



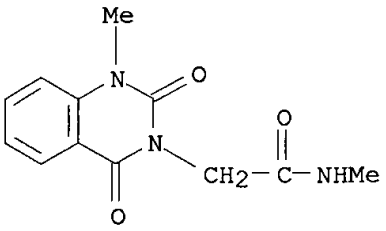
L20 ANSWER 54 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1987:568619 CAPLUS
DN 107:168619
TI Synthesis and anticonvulsant activity of some new 2,4-(1H,3H)-quinazolinedione derivatives
AU El Nasser Ossman, A. R.; Osman, A. N.; El-Helby, A. A.
CS Fac. Pharm., Al-Azhar Univ., Cairo, Egypt
SO Bulletin of Pharmaceutical Sciences, Assiut University (1986), 9(1), 105-18
CODEN: BPAUEC; ISSN: 1110-0052
DT Journal
LA English
AB I [R1 = Me or Et, R2 = CO2Et, oxiranyl, 2-(1-alkyl-2,4-dioxo-(1H,3H)-quinazolin-3-yl)-1-hydroxyethyl, CONHR3, (R3 = H, NH2, alkyl, PhCH2, cyclohexyl, PhCH2 or CH2CH2OH), CONHN:CHR4 (R4 = Ph or substituted phenyl)] were prepd. E.g., quinazolinedione K salts were **treated** with ClCH2CO2Et to give I (R1 = Me or Et, R2 = CH2CO2Et) (II and III, resp.). These were further **treated** with amines (to give I, R2 = CONHR3) or NH2NH2 (to give I, R2 = CONHNH2) which were **treated** with aldehydes to give I (R2 = CONHN:NCHR4). II and III were the most potent compds. when tested for anticonvulsant activity against pentylenetetrazole-induced **convulsion** in frogs.
IT **110679-29-3P 110679-30-6P 110679-31-7P**
110679-32-8P 110679-33-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and anticonvulsant activity of)
RN 110679-29-3 CAPLUS
CN 3(2H)-Quinazolineacetic acid, 1-ethyl-1,4-dihydro-2,4-dioxo-, ethyl ester (9CI) (CA INDEX NAME)



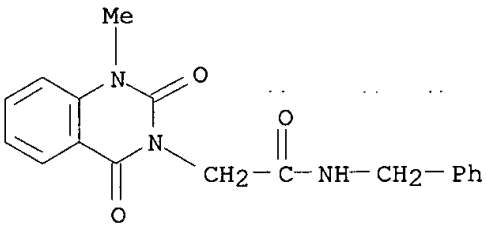
RN 110679-30-6 CAPLUS
CN 3(2H)-Quinazolineacetic acid, 1,4-dihydro-1-methyl-2,4-dioxo-, ethyl ester (9CI) (CA INDEX NAME)



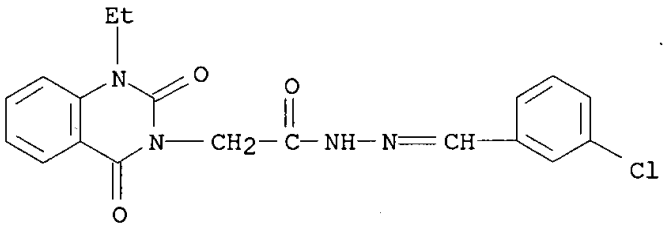
RN 110679-31-7 CAPLUS
CN 3(2H)-Quinazolineacetamide, 1,4-dihydro-N,1-dimethyl-2,4-dioxo- (9CI) (CA INDEX NAME)



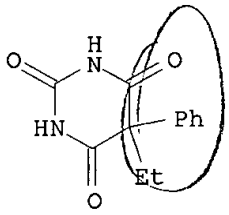
RN 110679-32-8 CAPLUS
CN 3(2H)-Quinazolineacetamide, 1,4-dihydro-1-methyl-2,4-dioxo-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



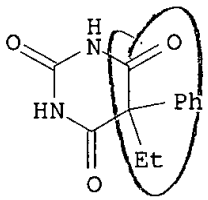
RN 110679-33-9 CAPLUS
CN 3(2H)-Quinazolineacetic acid, 1-ethyl-1,4-dihydro-2,4-dioxo-, [(3-chlorophenyl)methylene]hydrazide (9CI) (CA INDEX NAME)



L20 ANSWER 55 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1986:549 CAPLUS
DN 104:549
TI Reduced taurine contents and modification of anticonvulsive effects of phenobarbital and phenytoin by guanidinoethanesulfonate in mice
AU Izumi, Kanji; Kishita, Chikara; Nakagawa, Kazuo; Huxtable, Ryan J.; Shimizu, Takao; Koja, Takeshi; Fukuda, Takeo
CS Fac. Med., Kagoshima Univ., Kagoshima, 890, Japan
SO Progress in Clinical and Biological Research (1985), 179(Taurine: Biol. Actions Clin. Perspect.), 425-34
CODEN: PCBRD2; ISSN: 0361-7742
DT Journal
LA English
AB Guanidinoethanesulfonate (I) (1% soln. in drinking water for 9 days) decreased the taurine [107-35-7] levels in the brain of mice. I **treatment** had little or no effect on electroshock-induced tonic flexor (TF) and tonic extension (TE) reflexes in mice; the TE/TF ratio, a measure of seizure severity, was not affected by I. Both phenytoin [57-41-0] and phenobarbital [50-06-6] markedly decreased the TE/TF in mice with maximal electroshock **convulsions**. I **treatment** antagonized the effects of the anticonvulsant drugs on TE/TF ratio. The results indicate that phenytoin and phenobarbital provide protection against **convulsion**, at least in part, by increasing the taurine content in brain.
IT **50-06-6**, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(anticonvulsant activity of, taurine of brain in relation to)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)



L20 ANSWER 56 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1985:571923 CAPLUS
DN 103:171923
TI Convulsive thresholds and severity and the anticonvulsant effect of phenobarbital and phenytoin in adult rats administered 6-hydroxydopamine or 5,7-dihydroxytryptamine during postnatal development
AU Waller, Steven B.; Buterbaugh, Gary G.
CS Sch. Pharm., Univ. Maryland, Baltimore, MD, 21201, USA
SO Pharmacology, Biochemistry and Behavior (1985), 23(3), 473-8
CODEN: PBBHAU; ISSN: 0091-3057
DT Journal
LA English
AB Rats were given intracisternal 6-hydroxydopamine (6-OHDA) [1199-18-4] or 5,7-dihydroxytryptamine (5,7-DHT) [31363-74-3] within the 1st 3 postnatal days, at several ages centered on the 3rd postnatal week or on postnatal day 180. When the rats were 210-days-old, maximal electroshock **convulsive** thresholds and responses and the anticonvulsant effect of phenobarbital [50-06-6] and phenytoin [57-41-0] were detd. All 5,7-DHT **treatments** resulted in an approx. 21% decrease in the tonic **convulsive** threshold and increased the incidence of tonic hindlimb extension (HLE). Only the 5,7-DHT **treatment** at 180 days was assocd. with a more severe HLE response (shortened onset and prolonged duration). All neonatal 6-OHDA **treatments** were assocd. with no change in the tonic threshold, but increased the incidence and severity of HLE. The latter effect depended on the postnatal age of 6-OHDA-**treatment**: **treatment** at postnatal days 14 and 15 resulted in the greatest increase in severity (52% decrease in onset and 48% increase in duration). The 6-OHDA **treatment** to 180-day-old rats increased the incidence and duration of HLE but had no influence on the tonic threshold or onset of extension. The effectiveness of both phenobarbital and phenytoin to block HLE was variably decreased by all neurotoxin **treatments**. Apparently, interference with the postnatal maturation of monoaminergic influences on seizure processes can have a long-lasting influence on the ability of the brain to limit the generation and spread of seizure activity and on the effectiveness of anticonvulsant drugs.
IT **50-06-6**, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(anticonvulsant activity of, in senescence, after postnatal neurotoxic damage)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)

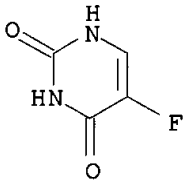


L20 ANSWER 57 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1985:464402 CAPLUS
DN 103:64402
TI General pharmacological properties of doxifluridine, a new fluorouracil derivative
AU Matsuura, Akihiro; Yajima, Takashi; Watanabe, Hiroshi; Furuya, Izumi; Tanaka, Yushiro; Umeda, Yukio; Takemoto, Chiori; Nakamura, Kazuo; Himori, Norio; Nakamura, Keiji
CS Dep. Pharmacol., Nippon Roche Res. Cent., Kamakura, 247, Japan
SO Oyo Yakuri (1985), 29(5), 803-31
CODEN: OYYAA2; ISSN: 0369-8033
DT Journal
LA Japanese
AB Doxifluridine [3094-09-5] (250,500, 1000 mg/kg orally), 5-fluorouracil (5-FU) [51-21-8] (62.5, 125, 250, 500 mg/kg orally), 5-deoxy-D-ribitol (Ro 17-8811) [13046-76-9] (500 mg/kg orally) and 5-deoxy-D-ribose (Ro 15-6702) [13039-75-3] (250, 500 mg/kg orally) had no significant effects on gross behavior, spontaneous activity, d-methamphetamine-induced locomotor behavior, or rectal temp. in mice and rats. Furthermore, doxifluridine did not alter the **convulsion** induced by metrazole, methylhexabital-induced hypnosis, or the licking response to hot-plate thermal stimulation in mice. Spontaneous EEG activity, arousal EEG responses to sensory stimulation (photic, tactile and odor) and spinal reflex potentials (mono- and poly-synaptic, and dorsal-root reflexes) in cats were not affected by i.v. doses of doxifluridine (10 or 30 mg/kg). Levallorphan challenge failed to provoke any abstinence syndromes in rats chronically **treated** with doxifluridine. Doxifluridine, 5-FU, Ro 17-8811, and Ro 15-6702 administered orally to dogs (30 mg/kg) did not produce abnormal behavioral change. Neither loose stools nor diarrhea was obsd. in dogs **treated** with any compds. employed. 5-FU alone, however, showed severe effects such as decreases in body wt. gain in mice and rats (at 1 wk after the **treatment**), and in temp. of the extremities in mice. Neither doxifluridine, 5-FU, Ro 17-8811, or Ro 15-6702 at 30 mg/kg produced significant effects on the blood pressure, heart rate, ECG, and respiration rate in conscious dogs. The inability of doxifluridine (10, 30, 100 mg/kg i.v.) to affect the respiratory and cardiovascular variables including myocardial contractile performance was confirmed also in pentobarbital anesthetized dogs. In addn., doxifluridine (30 mg/kg i.v.) did not modify the cardiovascular responses to i.v. noradrenaline (NE) acetylcholine (ACh), and bilateral carotid occlusion. Doxifluridine did not significantly alter renal function of either conscious rats loaded with 0.9% saline soln. (250, 500 mg/kg orally) or anesthetized dogs (10, 30 mg/kg i.v.). Gastrointestinal functions such as intestinal propulsive motility (mice) and bile flow (rats) were not modified following doxifluridine administration. Gastric acid secretion, however, was dose-dependently inhibited by intraduodenal doxifluridine (30, 100 mg/kg). Doxifluridine did not change either the pupil size (rats, 250, 500, 1000 mg/kg orally) or the nictitating membrane contraction (cats, 10, 30 mg/kg i.v.) and did not show local anesthetic activity in rats or infiltration anesthetic activity in guinea-pigs. As to the effects of doxifluridine (10-6-10-4M) on various isolated organs, the spontaneous contraction (frequency and contractile amplitude) of pregnant rat uterus was inhibited only at the highest concn. tested (10-4M), but the other prepns. such as guinea pig right atrium, ileum, and trachea, rat vas deferens, nonpregnant rat uterus and rat stomach did not abnormally respond to doxifluridine. The results indicate that doxifluridine is well tolerated by the exptl. animals and exerts almost no serious effects on the central, somatic or autonomic nervous system,

cardiovascular and respiratory system, renal function, gastrointestinal function, or isolated muscle prepns.

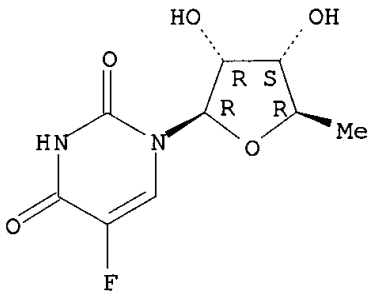
IT **51-21-8 3094-09-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(pharmacol. of)

RN 51-21-8 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 5-fluoro- (9CI) (CA INDEX NAME)

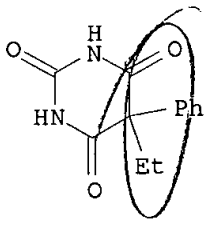


RN 3094-09-5 CAPLUS
CN Uridine, 5'-deoxy-5-fluoro- (8CI, 9CI) (CA INDEX NAME)

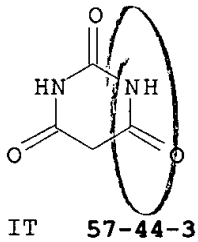
Absolute stereochemistry.



L20 ANSWER 58 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1985:215116 CAPLUS
DN 102:215116
TI Modification of the antiepileptic actions of phenobarbital and phenytoin by the taurine transport inhibitor, guanidinoethane sulfonate
AU Izumi, Kanji; Kishita, Chikara; Nakagawa, Kazuo; Huxtable, Ryan J.; Shimizu, Takao; Koja, Takeshi; Fukuda, Takeo
CS Fac. Med., Kagoshima Univ., Kagoshima, 890, Japan
SO European Journal of Pharmacology (1985), 110(2), 219-24
CODEN: EJPHAZ; ISSN: 0014-2999
DT Journal
LA English
AB Whether chronic administration of guanidinoethane sulfonate [543-18-0], an inhibitor of taurine [107-35-7] uptake, could modify the antiepileptic actions of phenobarbital [50-06-6] and phenytoin [57-41-0] on maximal electroshock seizures was investigated in mice. **Treatment** with 1% guanidinoethane sulfonate decreased the taurine concn. in the brain to 76% of the control value. Under these conditions, neither the severity of tonic **convulsions** of maximal electroshock seizures nor the threshold for tonic extension caused by electroshock was altered. However, **treatment** with guanidinoethane sulfonate lessened the antiepileptic actions of phenobarbital and phenytoin on electroshock seizures. The brain concns. of phenobarbital and phenytoin were unaltered by administration of guanidinoethane sulfonate. The brain concns. of guanidinoethane sulfonate and total guanidino compds. were unchanged by the injection of either phenobarbital or phenytoin. It is suggested that the obsd. loss of anticonvulsive potency of phenobarbital and phenytoin may have been related to the decrease in taurine concn. produced by guanidinoethane sulfonate.
IT **50-06-6**, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(anticonvulsant activity of, brain taurine decrease by guanidinoethanesulfonate effect on)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)

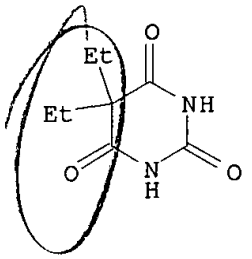


L20 ANSWER 59 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1983:433024 CAPLUS
DN 99:33024
TI Interaction between spontaneous and electrically induced **convulsions** and their short- and long-term effects in the abstinence after chronic barbital **treatment** in the rat
AU Wahlstroem, Goeran
CS Dep. Pharmacol., Univ. Umeaa, Umeaa, S-901 87, Swed.
SO Brain Research (1983), 266(2), 225-32
CODEN: BRREAP; ISSN: 0006-8993
DT Journal
LA English
AB Male rats were **treated** with barbital (I) [57-44-3] supplied in their drinking water (daily dose around 200 mg/kg) for 50 wk. When the **treatment** was stopped (day 0) spontaneous **convulsions** were monitored for the first 3 days of the abstinence. On day 3 a **convulsion** was induced by electricity in half of the rats (controls and barbital-**treated**) and 1 h later the sensitivity to hexobarbital was detd. with a threshold test. Sensitivity to hexobarbital was then tested in the same manner at approx. weekly intervals for the first 110 days of the abstinence. On day 3 of the abstinence a tolerance to hexobarbital [56-29-1] (45% increase in threshold above controls) and a reduced threshold to induce **convulsions** with electricity (-27% compared with controls) was seen in previously barbital-**treated** animals. Spontaneous or induced **convulsions** occurring prior to the hexobarbital threshold detn. decreased the tolerance to the same extent (-22 to -28%). On day 28 rats with no **convulsions** up to day 3 had a marked renewal of tolerance to hexobarbital (29% increase above controls), while rats with **convulsions** recorded up to day 3 had less or no such tolerance. There was a pos. correlation between the hexobarbital thresholds in barbital-**treated** rats recorded on day 3 and on day 28. Later in the abstinence, barbital-**treated** rats with **convulsions** prior to day 3 tended to have a hexobarbital threshold slightly but significantly elevated compared with the controls (10-15%). This change could be a sign of a long-lasting increased excitation.
IT **67-52-7D**, derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(anticonvulsant activities of, dependence and tolerance in relation to)
RN 67-52-7 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione (9CI) (CA INDEX NAME)

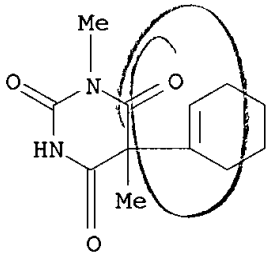


IT **57-44-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(anticonvulsant activity of, dependence and tolerance in relation to)

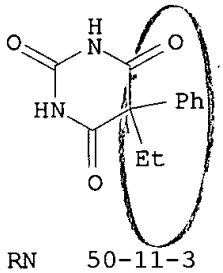
RN 57-44-3 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5,5-diethyl- (9CI) (CA INDEX NAME)



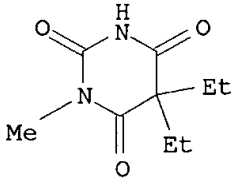
L20 ANSWER 60 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1982:45895 CAPLUS
DN 96:45895
TI Pharmacological activity and toxicity of Hexenal, Corazole and ethylmorphine in experimental hypokinesia
AU Khakimov, Z. Z.; Kamarin, A. S.; Nadzhimutdinov, K. N.
CS Med. Inst., Tashkent, USSR
SO Meditsinskii Zhurnal Uzbekistana (1981), (10), 56-60
CODEN: MZUZA8; ISSN: 0025-830X
DT Journal
LA Russian
AB hexenal (I) [56-29-1], corazole (II) [54-95-5], and ethylmorphine (III) [76-58-4] showed enhanced pharmacol. activity (sleep, **convulsant**, and analgetic, resp.) and enhanced toxicity in rats subjected to 3-30 days of hypokinesia. Apparently, a loss of liver metabolic activity produced by the hypokinesia leads to enhanced drug activity and toxicity. This effect may be significant in the **treatment** of patients with drugs deactivated by liver metab.
IT **56-29-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(pharmacol. of, in hypokinesia)
RN 56-29-1 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-(1-cyclohexen-1-yl)-1,5-dimethyl- (9CI) (CA INDEX NAME)



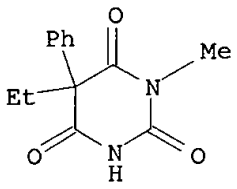
L20 ANSWER 61 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1980:33789 CAPLUS
DN 92:33789
TI Anticonvulsants. 1. Effect of the lipophilicity on anticonvulsive and neurotoxicity potentials
AU Lehmann F., Pedro A.
CS Dep. Farmacol. Toxicol., Cent. Invest. Estud. Avanzados, Mexico City, Mex.
SO Revista de la Sociedad Quimica de Mexico (1979), 23(2), 94-6
CODEN: RSQMAN; ISSN: 0583-7693
DT Journal
LA Spanish
AB Regression anal. of available data for 13 anticonvulsants revealed correlations between lipophilicity and relative potencies (protection against electroshock-induced **convulsions**, protection against pentylenetetrazole **convulsions**, and ataxia - a neurotoxicity symptom). The results suggested that for compds. of low lipophilicity, an ED will also be toxic and that high lipophilicity will be assocd. with a high **therapeutic** margin.
IT **50-06-6**, biological studies **50-11-3 115-38-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(anticonvulsant activity of, lipophilicity and neurotoxicity in relation to)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)



RN 50-11-3 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5,5-diethyl-1-methyl- (9CI) (CA INDEX NAME)



RN 115-38-8 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-1-methyl-5-phenyl- (9CI) (CA INDEX NAME)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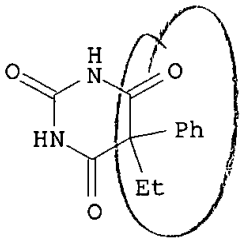
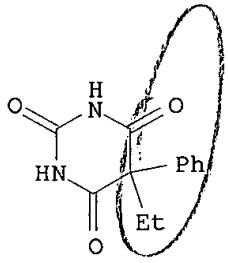
L20 ANSWER 62 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1974:10668 CAPLUS
DN 80:10668
TI Effect of anabolic hormones on the spasmodic syndrome under experimental and clinical conditions
AU Maleva, I. F.
CS Ryazan, USSR
SO Trudy Moskovskogo Nauchno-Issledovatel'skogo Instituta Psikhiatrii (1972), 64, 171-4
CODEN: TMIPB7; ISSN: 0371-9677
DT Journal
LA Russian
AB Retabolil (I) [360-70-3] given i.m. to dogs at 1 mg/kg once every 3 days for a total of 3 injections did not alter corazole-induced **convulsions**, but when combined with phenobarbital (II) [50-06-6] (10 mg/kg) improved the anticonvulsant effect of the latter. I also improved the condition of epileptics when given i.m. at 3-day intervals against a background of anticonvulsive and neuroleptic **therapy**.
IT **50-06-6**, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(anticonvulsant activity of, retabolil enhancement of)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)



L20 ANSWER 63 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1973:132049 CAPLUS
DN 78:132049
TI Influence of the inhibitor of dopamine-.beta.-hydroxylase diethyldithiocarbamate (DDC) on the anticonvulsive activity of certain anticonvulsants
AU Rusinov, K. S.; Georgiev, V. P.
CS Inst. Physiol., Sofia, Bulg.
SO Doklady Bolgarskoi Akademii Nauk (1973), 26(1), 141-4
CODEN: DBANAD; ISSN: 0366-8681
DT Journal
LA English
AB In rats with s.c. pentylenetetrazole (I) [54-95-5]-induced **convulsions**, the latency periods of the seizures were lengthened in animals **treated** with Phenurone [63-98-9] and esp. with Metatolylcarbamide after preliminary administration of diethyldithiocarbamate (DDC) [147-84-2]. After timed i.v. infusion of pentylenetetrazole, the anticonvulsant effect of Metatolylcarbamide was essentially not influenced by DDC. The effect of phenobarbital (II) [50-06-6] was potentiated by DDC with respect to thresholds for general excitation and the clonic phase of the seizure. The effect of Phenurone was potentiated by DDC in regard to the 3 phases of the seizure. After s.c. administration of strychnine [57-24-9], DDC potentiated the anti-strychnine effect of Metatolylcarbamide, decreasing the percentages of animals affected by **convulsions** and increasing survival time. DDC potentiated the protective effect of all 3 anticonvulsants after timed i.v. infusion of strychnine. The potentiating effect of DDC in relation to the anticonvulsants was more marked than the antistrychnine effect of DDC alone.
IT **50-06-6**, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(anticonvulsant activity of, diethyldithiocarbamate potentiation of)
RN 50-06-6 CAPLUS
CN 2,4,6(1H,3H,5H)-Pyrimidinetrione, 5-ethyl-5-phenyl- (9CI) (CA INDEX NAME)



L20 ANSWER 64 OF 64 CAPLUS COPYRIGHT 2003 ACS
AN 1968:38049 CAPLUS
DN 68:38049
TI Pharmacological studies on 5-fluorouracil
AU Aratani, Harue; Yamanaka, Yasumitsu; Onishi, Reiko; Kono, Shizuko; Higaki, Yuzaburo
CS Hiroshima Univ. Sch. Med., Hiroshima, Japan
SO Chemotherapy (Tokyo) (1967), 15(5), 519-26
CODEN: NKRZAZ; ISSN: 0009-3165
DT Journal
LA Japanese
AB The mouse LD50 values for 5-fluorouracil via intracerebral, s.c., and i.p. routes were 41.6, 730, and 1010 mg./kg., resp. An intracerebral dose of 18.15 mg./kg. caused chronic **convulsion**, lateral turning, and whole-body rotation in mice. Subacute toxicity studies demonstrated that 50% of the rats died in 30-40 days when given 20 mg./kg./day, and 10-50% died in 50-60 days when given 5-10 mg./kg./day. Rats exposed to subacute toxic doses of 5-fluorouracil showed decreased testis wt. and increased spleen wts. Movement of isolated frog heart was stimulated by 0.2 mg. 5-fluorouracil per ml. and was inhibited by 2 mg./ml. Contraction of isolated rabbit intestine was stimulated by 1 .mu.g. 5-fluorouracil per ml. but was inhibited by 0.5 mg./ml. The drug was without an effect on the perfusate flow rates in the vessels of isolated auricles, while it increased vessel permeability in isolated rabbit skin at concns. of 1 mg./ml. The drug caused a transient fall in blood pressure and a decrease in respiration in urethan-anesthetized rabbits at 4 mg./kg., and tachycardia was seen at 20 mg./kg. Thus, 5-fluorouracil does not posses favorable pharmacol. actions at **therapeutic** doses.
IT **51-21-8**
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(pharmacology of)
RN 51-21-8 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 5-fluoro- (9CI) (CA INDEX NAME)